

8. Project Strategic Plan

Introduction

a. The Northwest Regional Biocontainment Laboratory (NWRBL) will be an essential component in the national biodefense network of research programs to combat infectious disease threats to the population. The Pacific Northwest region possesses unique strengths in biotechnology platforms, including genomics, proteomics, and bioinformatics. Furthermore, centering an RBL at the University of Washington (UW) is logical since the Seattle biomedical community occupies an international leadership position in infectious diseases research. The Infectious Disease research program has been a strong traditional emphasis of the UW Medical School. The School's training programs in infectious diseases, microbiology, and immunology are highly successful, interactive, and comprehensive. The UW currently has five NIH funded training grants in infectious diseases research that have trained hundreds of individuals over the last 25 years, many of them now leaders in the field. Infectious diseases research at the UW permeates many of the clinical and basic science departments, including Medicine, Pediatrics, Genome Sciences, Microbiology, Immunology, Biochemistry, and Structural Biology. Currently, more than three hundred trainees are engaged in infectious disease research in these departments. Furthermore, these departments host a variety of centers and cooperative research programs studying infectious diseases, most notably the WWAMI Regional Center of Excellence for Biodefense and Emerging Infectious Diseases (Fig. 1). Other centers include the Center for AIDS Research and the Sexually Transmitted Diseases Cooperative Research Center, both directed by Dr. King Holmes, AIDS Vaccine Evaluation Unit directed by Dr. Julie McElrath, the Cooperative Research Center for Structural Genomics of Pathogenic Protozoa directed by Dr. Wim Hol, and the Cystic Fibrosis Research and Development Program directed by Dr. Samuel Miller (which includes the Cystic Fibrosis Foundation funded program for post-genomic evaluation of *Pseudomonas aeruginosa* infection of Cystic Fibrosis (CF) airways) and the Keck Center for Microbial Pathogenesis. These centers involve cooperative research consortia that have been assembled from a variety of departments to study specific infectious disease problems. The cooperative research culture and environment at the UW is ideal for the deployment of an RBL, since a cooperative spirit and culture will be required to successfully achieve the programmatic goals of the NIAID.

There are many institutions in the region with established connections to the UW that also have strong microbiology and infectious diseases research programs. These institutions include the Fred Hutchinson Cancer Research Center, the Children's Hospital and Regional Medical Center, the Institute for Systems Biology, the Rocky Mountain Laboratories of the NIAID, and the Seattle Biomedical Research Institute among others. The Pacific Northwest (and specifically Seattle) is one of the centers in the United States for biotechnology companies, many of which focus on infectious diseases and inflammation research, including Corixa, Chiron (formerly Pathogenesis), Micronics, and Amgen (formerly Immunex). Their presence will facilitate the translation of discoveries emerging from the RBL into practical vaccines and therapeutics. Additionally, the medical school consortium called the WWAMI Program links the UW with medical education in Idaho, Alaska, Montana, and Wyoming, providing an established network for regional education and training, as well as excellent opportunities for future growth of an RBL (Fig. 1). The WWAMI partners occupy greater than one-quarter of the landmass of the United States. The geography of the WWAMI region is also uniquely important for biodefense in that it is situated on the western coast

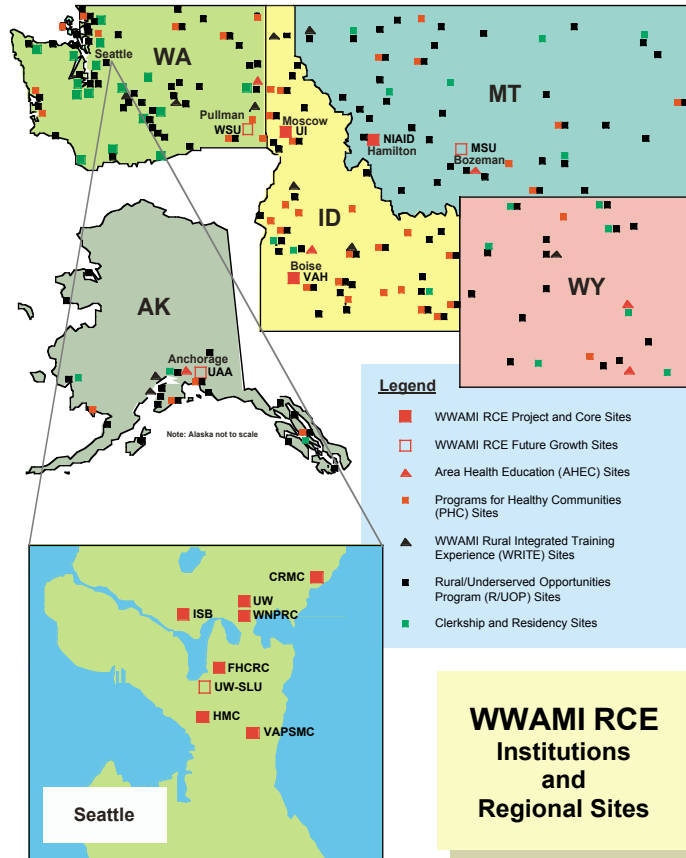


Figure 1. Map of WWAMI consortium showing RCE Project and Core Sites.

Fig. 1 Map of WWAMI consortium showing RCE Project and Core sites.

of the United States, bordering Canada and serving as a transportation portal to Asia. This unique group of WWAMI-associated institutions forms a powerful base of resources to support the proposed NWRBL (see table 1 and Letters of Support). As a central hub in this network of affiliations, and as a leader in infectious diseases research, the UW is clearly an ideal institution to host a Regional Biocontainment Laboratory.

The NWRBL will be a leading edge facility that will advance the infectious disease research goals of the Pacific Northwest and nation. The UW Capital and Space Planning Office, in conjunction with the campus Architect/Planner, identified a campus site based upon proximity to existing similar research, program functionality, life-safety for employees, public safety, and, security. Security of the site and building components was given a #1 priority based on the NIH requirement that the facility house Select Agents, identified as category A, B, and C priority pathogens. This advanced technology facility will meet or exceed Federal, state, and local standards for protecting laboratory workers and the environment, and maximizes the capacity of the site to provide space for affiliate infectious disease research programs in Genome Sciences, Division of Allergy & Infectious Diseases, Immunology, Microbiology, Medical Genetics, and the schools of Pharmacy and Public Health/Community Medicine. Such a facility will increase the University's ability to recruit new faculty to the region and attract new Biodefense and Emerging Infectious Disease research programs.

Table 1. The NWRBL will accelerate research at the following regional institutions and companies

- **University of Washington School of Medicine Seattle, WA**
- **Washington National Primate Research Center Seattle, WA**
- **VA Puget Sound Medical Center, Seattle WA**
- **Harborview Medical Center, Seattle, WA**
- **The Fred Hutchinson Cancer Research Center, Seattle, WA**
- **The Institute for Systems Biology, Seattle, WA**
- **Children's Regional Medical Center, Seattle, WA**
- **Washington State University, Pullman, WA**
- **Oregon Regional Primate Research Center, Beaverton, OR**
- **NIAID Rocky Mountain Laboratories, Hamilton, MT**
- **Seattle Biomedical Research Institute**
- **Montana State University, Bozeman MT**
- **Amgen, Seattle, WA**
- **Corixa, Inc. Seattle, WA and Hamilton, MT**
- **Corus Pharma Inc., Seattle, WA**
- **Micronics, Incorporated, Redmond, WA**
- **University of Idaho, Moscow, ID**
- **Oregon Health & Science University, Portland, OR**
- **Boise Veterans Affairs, Boise, ID**
- **Oregon State University, Corvallis, OR**
- **University of Oregon, Eugene, OR**
- **University of Wyoming, Laramie, WY**
- **University of Alaska, Fairbanks, AK**

The design provides efficient, useful space for investigators and administrative staff, a comprehensive animal facility, with both barrier and containment animal housing, and procedure rooms. Space has been allocated for a secure computer server that will not be accessible outside the facility. Office space is also provided for the UW's Responsible Official, who is required by the Federal government to maintain detailed and secure records to track the Select Agents. Office and laboratory spaces will be available to support scientists from other sites and partners in the region who may conduct research on site. The design of research laboratory space includes suites of Biological Safety Level 3 (BSL-3), as well as Biological Safety Level 2 (BSL-2). Support spaces include a Good Laboratory Practice (GLP) pilot plant to produce vaccine for Phase 1 clinical trials. The Core Instrument suite will house large shared equipment such as MRI Imaging, Confocal Microscopy, Fluorescence Activated Cell Sorter, Robotics, and Transmission Electron Microscopes. The design combines all animal holding, animal procedure rooms, and Necropsy rooms, so the animals are not transported outside the viaticum to laboratory spaces. Due to the unique engineering aspects of this facility, it is anticipated that an office be allocated for a Building Engineer.

Planned activities

After submission of the application, the Scientific Oversight Committee (see below) will meet to begin the process of identifying faculty and programs that could benefit from the unique capabilities of the NWRBL. It is anticipated that the WWAMI RCE will take a large role in occupying the facility. Additionally, as the WWAMI RCE matures and takes on broader scopes of activity, new research directions will be identified and accelerated

to the grant proposal stage in order to take full advantage of the NWRBL. The planned technological sophistication of the NWRBL will fill unmet needs in the region and will allow, among others, the following types of activities:

<u>Capability</u>	<u>Research need met</u>
Whole small animal MRI	test/develop new models of disease
Pilot plant	vaccine development and production
BSL-3 robotics	high-throughput screening of live select agents
ABSL-3 vivarium	expansion of risk group 3/small animal research
Nonhuman primate housing	preclinical vaccine trials
N + 1 redundancy	uninterrupted research timelines

The NWRBL will also enter into collaborative relationships with the regional biotechnology sector and faculty of the neighboring Department of Bioengineering in order to make progress toward the development and validation of detection/diagnostic devices. During the design phase, it is expected that there will be the possibility to add or modify capabilities to the Laboratory as research objectives evolve. Active participation of the Committee from the early going will be instrumental in taking advantage of these opportunities. Also, specific mechanisms for seeking out new research partnerships in the region and making the NWRBL available to these initiatives is described in section **d**.

Organizational structure of the NWRBL

The NWRBL will be headed by Paul G. Ramsey, Principal Investigator and Dean of the Medical School at the University of Washington. Dr. Ramsey trained as an Infectious Disease physician prior to his assumption of administrative duties as Dean. Dr. Ramsey holds the authority to allocate resources and make programmatic decisions in regard to the conduct of the NWRBL. The Dean of the Medical School is responsible to the Provost (Thorud), who in turn serves the president of the University, Mark Emmert (Figure 2). President Emmert has recently been recruited to the UW, and has endorsed an active campaign of attracting state, federal, and local funding to the UW in his first public address to the campus community on 11/30/04.

Administration of the NWRBL on behalf of Dr. Ramsey will be accomplished by three committees, each dedicated to core aspects of management of the NWRBL. The **Scientific Oversight Committee** will be charged with scientific guidance (including attracting and assigning researchers within the Laboratory), fiscal oversight of the scientific operations of the Laboratory as a shared resource, and stewardship of interactions with the community and broader public through a Public Relations function.

Reporting to the Scientific Oversight Committee will be two additional bodies, the **Construction Committee** and the **Facility Operation Committee**. It is inherent in the conception of this structure that the Construction Committee will be the most active during the design and building phase, while gradually yielding executive function to the Facilities Operation Committee as the project nears completion. To this end, there will be significant overlap in the constituencies of these committees to lend continuity of experience while the individuals involved begin to take on the functions of a fully operational laboratory. The double-headed arrows used in the organizational diagram emphasize this point as well as the idea of freely flowing information between these bodies. Since an unusual degree of Federal, State, and local requirements will impinge upon the construction and use of this landmark facility, a correspondingly exceptional exchange of information between these groups is seen as essential for successful achievement of the aims of the NWRBL.

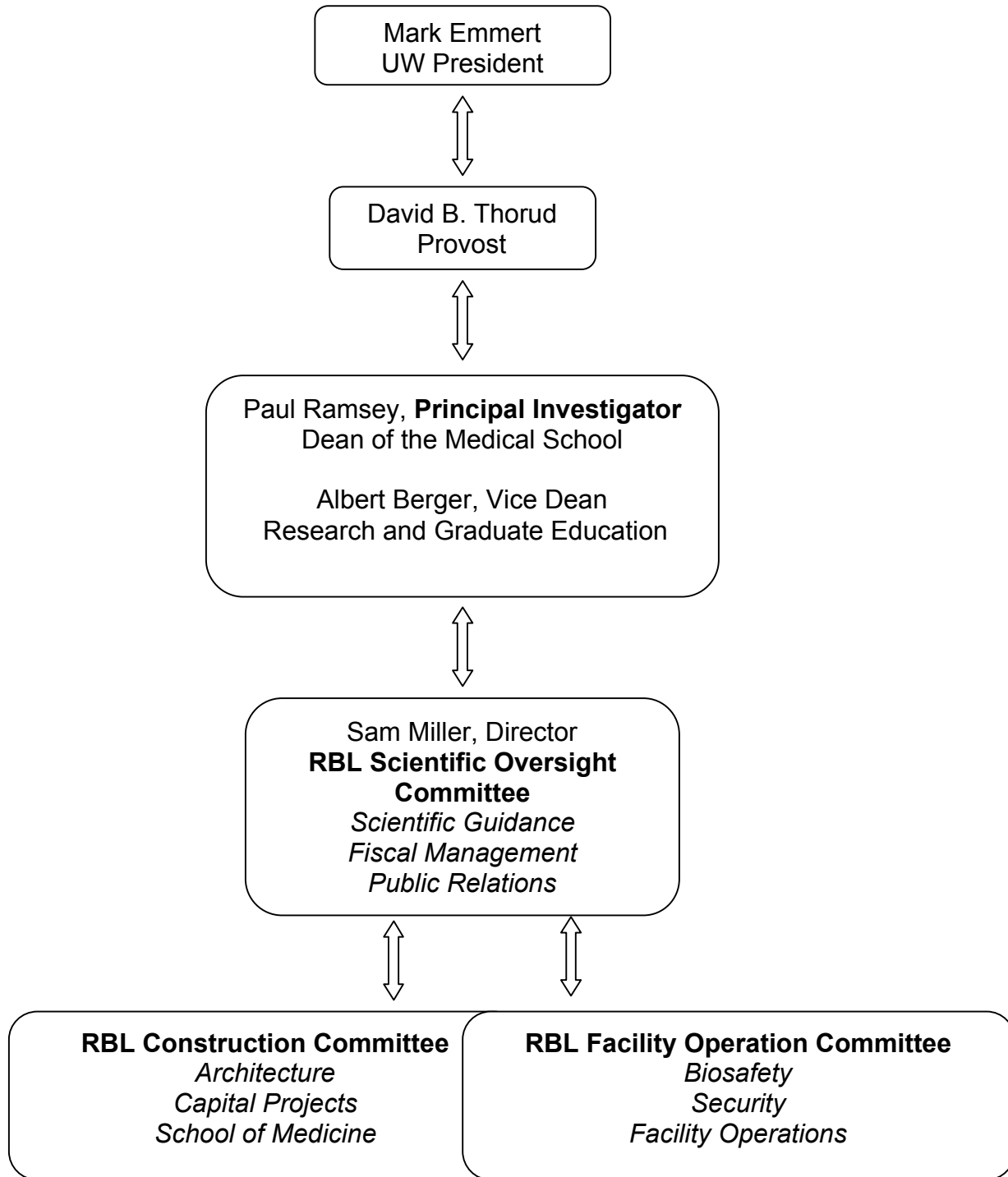


Figure 2. Proposed organizational structure of the NWRBL

The Scientific Oversight Committee will consist of the following individuals from the University of Washington:

NWRBL Scientific Oversight Committee:

Samuel I. Miller, Director	PI & Director, WWAMI Regional Center of Excellence for Biodefense and Emerging Infectious Diseases
William J. Bremner	Chair, Department of Medicine
Christopher B. Wilson	Chair, Department of Immunology
E. Peter Greenberg	Chair, Department of Microbiology
Robert H. Waterston	Chair, Department of Genome Sciences

The placement of these individuals on the Scientific Oversight Committee gives strong representation on the part of relevant departmental stakeholders in the NWRBL. In this way, coordination of multiple needs for access to the completed facility will be built into the organizational structure. The director of this committee, Samuel Miller, will communicate its findings to the PI Paul Ramsey. Albert Berger, Vice Dean for Research and Graduate Education, will help to ensure regular access to the Office of the Dean. In addition, administrative support will be provided to the Committee to aid in the execution of its duties in the pre-award, design & construction, and post-commissioning phases of the NWRBL.

As described earlier, the Scientific Oversight Committee will coordinate the efforts of the Construction Committee and the Facility Operations Committee. Upon Award, both of these committees will be convened, although the Construction Committee will be the most active early on. This Committee will be comprised of institutional members of UW building committees plus a number of uniquely seated individuals who will add the necessary assurances that the physical construction of the Regional Biological Laboratory meets all stated regulatory and programmatic goals. The members of the Construction Committee will be as follows:

NWRBL Construction Committee:

Albert J. Berger	Vice Dean, Office of Research and Graduate Education School of Medicine
Samuel I. Miller	Professor, Division of Allergy & Infectious Diseases School of Medicine, Director, WWAMI RCE
Tye V. Minckler	Director of Facilities Development and Management, School of Medicine
Stephanie K. Steppe	Director, Health Sciences Academic Services & Facilities
John C. Chapman	Director, Campus Engineering and Operations, Facilities Services
Karen A. VanDusen	Director, Environmental Health and Safety Responsible Official, Select Agent Program

Vicky Stormo	Chief, University of Washington Police
Lee Copeland	UW Architectural Adviser, Weinstein Copeland Architects
Doug Holen	Director Capital Projects South - Capital Projects Office
Colleen Pike	Acting Director - Capital & Space Planning Office.

The **Facility Operations Committee** will coordinate implementation of biosafety practices, security, and the day-to-day operations of the NWRBL. This committee will aid in identifying physical resources to the Scientific Oversight Committee in order to help in priority setting, scheduling, and granting access to facilities by investigators in the region. In addition, this committee will oversee security and biosafety training of all individuals with access to the NWRBL. In conjunction with the University of Washington Department of Environmental Health and Safety (EH&S), this body will assure that researchers and support staff meet regulatory and practice standards in order to protect the community and workplace and to provide a safe and healthful facility. This will be accomplished through frequent review and testing of training procedures, and insistence upon stringent levels of compliance.

NWRBL Facility Operations Committee:

Samuel I. Miller Professor	Division of Allergy & Infectious Diseases School of Medicine
Vicky Stormo	Chief, University of Washington Police
Karen A. VanDusen	Director, Environmental Health and Safety Responsible Official, Select Agent Program
Julie Reid	Director, Departmental Support, Dean's Office, School of Medicine
John C. Chapman	Director Campus Engineering and Operations - Facilities Services

b. The NWRBL will have a unique working relationship with the WWAMI Region X RCE.

The WWAMI RCE. The University of Washington and surrounding research community is significantly invested in infectious disease research. Foremost among the biodefense-related research activities is the Region X WWAMI Regional Center of Excellence for Biodefense and Emerging Infectious Disease. Directed by Samuel Miller. The WWAMI RCE is awarded \$11,677,224 by NIAID in 2004. The WWAMI RCE is a highly integrated center, with the majority of its research projects concentrated in institutions in the Seattle area. The involvement of the RCE Director Sam Miller in the NWRBL offers a preexisting mechanism for exploiting the highly collaborative interactions of the infectious disease researchers that make up the RCE. Through its interactions with regional investigators and the seeding of developmental projects throughout the area, this network also brings Northwest researchers and their institutions into a working relationship. It is likely that researchers from the RCE and in the region

Virulence Factors in the Airway
9/4/03-2/29/08

Project 4
U54 AI057141

PI: Nina Salama
\$1,367,483

Genes that are both expressed and required during infection are the best targets for vaccines or antimicrobial therapy. Similarly, antimicrobial drugs target processes (both *in vivo* and *in vitro*) essential for bacterial survival, e.g., DNA replication, RNA transcription and protein synthesis. In this Project a whole-genome approach will be used to identify essential genes *in vitro*, and also those specifically expressed and required *in vivo*. *Yersinia pestis* (human strain CO92), for which there exists a complete annotated genome sequence, animal models, and vectors for transposon mutagenesis, is the first target of study. Whole-genome cDNA microarray sequences that contain all predicted open reading frames will be constructed and used to study transcription *in vitro* and *in vivo*, and to track transposon mutants during infection. Genes which are upregulated *in vivo* will be identified using the rat bubo model. Pools of mutants that have a phenotype in the rat bubo model and/or the mouse pulmonary model will be tested in a primate model of pulmonary infection to identify genes most important during human infection. As progress is made, similar techniques will be applied to other potential agents of bioterrorism, specifically *Francisella tularensis*.

Bacterial Lipopolysaccharide Structure
9/4/03-2/29/08

Project 6

P.I. Robert Ernst
\$1,581,086

U54 AI057141

Bacterial pathogens have evolved adaptive responses to environmental changes encountered when they enter a host from an external reservoir. Modifications to essential cell membrane components such as lipid A are important for pathogenesis. Preliminary studies have indicated that temperature-dependent alteration of lipid A structure upon entry into the mammalian host may represent a pathogenesis strategy common to the *Yersiniae*. This project will define and elucidate the mechanism of synthesis of environmentally-regulated lipid A structures from *Yersinia pestis*, and also define the lipid A structures of *Francisella tularensis* and *Burkholderia pseudomallei*. In addition, the role of these structures in affecting the innate immune system of the host will be determined. Experiments will 1) characterize environmentally-regulated LPS structures of *Y. pestis* and other gram-negative agents, 2) define genes important to environmentally-regulated LPS structures of *Y. pestis* and other gram-negative agents, 3) define genes important to modification of lipid A and polymyxin resistance of *Y. pestis* and other gram-negative agents, 4) define the role of these genes in resistance to antimicrobial peptides, stimulation of host inflammation, and mouse virulence.

Development and assessment of novel biodefense vaccine technologies

Project 7

P.I. Carolyn J. Hovde

9/4/03-2/29/08

U54 AI057141

\$1,748,409

This project will rely on recent advances in vaccine and adjuvant technologies and on critical understanding of the innate immune system in order to develop or improve immunization methods for biodefense purposes. *Yersinia pestis* will be used as the model for developing these methods, relying on the experience of the research group with *Yersinia* pathogenesis. However, it is expected that experimental results will be broadly applicable to all Gram-negative biothreat agents under investigation at the WWAMI RCE. The research will focus on protection against *Y. pestis* in murine and primate infection models, and the technologies that are most effective against this organism will be applied to animal models for *Francisella tularensis* and *Burkholderia pseudomallei*. Experiments will be undertaken to: 1) assess the efficacy of innate immune system stimulation to protect against aerosolized *Y. pestis*, 2) assess the ability of novel adjuvants to enhance protection with *Y. pestis* subunit and live attenuated

vaccine candidates, 3) identify genetic loci affecting *Y. pestis* virulence for development of an attenuated vaccine, and 4) apply the knowledge obtained in these *Y. pestis* studies to enhance innate and specific immunity towards *B. pseudomallei* and *F. tularensis*.

A Rat Model to Study Bubonic Plague Lymphadenitis

Project 8

9/4/03-2/29/08

U54 AI057141

**PI: B. Joseph Hinnebusch
(Intramural Research Project)**

The overall objective of this project is to develop appropriate animal models for plague, to use them to identify and investigate the role of specific *Y. pestis* virulence and transmission factors, and to characterize the host response to naturally acquired infection. The ultimate goal is to use the animal models to identify new targets for medical countermeasures against plague and to test the efficacy of novel plague vaccines and delivery systems. Experience gained from the rat model will also help guide the development of nonhuman primate models for plague. An established lymphadenitis model may be applicable to other invasive Gram-negative Class A agents such as *Francisella tularensis*, which, like *Y. pestis*, causes pronounced lymphadenopathy. The initial approach will be to Establish a rat model for bubonic and pneumonic plague. A genomic approach will be used to Identify *Y. pestis* genes required for the pathogenesis of lymphadenitis (bubo formation) following flea-borne transmission. Lastly, experiments will characterize the rat humoral immune response to infection and the *Y. pestis* antigens produced in the infected lymph node (bubo).

Innate Immunity to Pneumonic Plague Project 9

9/4/03-2/29/08

U54 AI057141

**PI: Shawn Skerrett
\$1,531,318**

The overall goal of this project is to define molecular pathways involved in the activation of innate immunity to airborne infection with gram negative bacteria that are potential biological weapons, including the agents of plague (*Yersinia pestis*), tularemia (*Francisella tularensis*) and melioidosis (*Burkholderia pseudomallei*). Aerosol challenge models will be used in genetically modified mice to explore the roles of Toll-like receptors (TLRs) and cell populations in mediating inflammatory and immune responses to live bacteria and selected bacterial ligands. The specific aims of the project are to determine the role of MyD88 in mediating innate immunity to aerosolized pathogens, determine the role of TLR4 and TLR2 in mediating innate immunity, and investigate the role of bone marrow-derived cells and respiratory epithelial cells in the activation of innate immune responses to *Y. pestis*.

Variation in Human Innate immunity Project 11

9/4/03-2/29/08

U54 AI057141

**PI: Tom Martin
\$6,482,078**

This project focuses on identifying the factors that determine human susceptibility to biothreat agents, to be able to identify high-risk groups in order to target effective preventive measures. An understanding of the molecular mechanisms underlying human variability in innate immune inflammatory responses to these agents may help to prospectively identify populations at high-risk for poor outcomes after a release. Experiments will measure the variability in innate immune responses to *Y. pestis* and other select agents using an *in vitro* model of whole blood responses to bacterial products. The magnitude of the genetic component of this variability will be investigated through a classical twins study, and the extent to which specific allelic haplotypes contribute to this variability will be determined. Finally, we will identify innate immune response profiles in patients with chronic respiratory diseases, a population that is likely to be at high-risk for a poor outcome after exposure.

WWAMI RCE Cores The WWAMI RCE is also composed of ten cores that provide administrative and technical research support to the activities of the RCE. The NWRBL would provide an opportunity to coordinate a number of these cores in one physical space, offering significant cross-platform savings in time and translational efficiency. For example, advances made by the Bioinformatics core would be immediately applicable to proteomic analyses in the Mass Spectrometry core. The cores are as follows:

Core	PI	total award
Nonhuman Primate Studies	William R. Morton	\$7, 608,884
DNA Sequencing	Maynard Olson	\$6,250,202
Mass Spectrometry	David Goodlett	\$4,310,530
Pulmonary Infection and Inflammation	Shawn Skerrett	\$1,826,728
Data Integration and Bioinformatics	Mitch Brittnacher	\$1,850,232
Microarray Analysis	Nina Salama	\$1,456,440
Training and Education	John Coombs	\$ 1,669,968
Bacterial Strains	Colin Manoil	\$374,313
<i>Yersinia pestis</i> Biology	Joe Hinnebusch	(intramural)
Administration	Sam Miller	\$4,349,607

WWAMI RCE Developmental Projects In addition to the previously described research projects and cores, the WWAMI RCE also awards Developmental Projects grants to researchers in the region working on category A, B, & C priority pathogens. The currently awarded grants are:

PI	Title	Institution
Karen Guillemin	Microbiota protection against <i>Salmonella</i> infection	University of Oregon
David Pascual	M cell delivery platform for plague	Montana State University
Gregory Bohach	Host and <i>Yersinia</i> adaptational responses	University of Idaho
Dennis Stevens	Innate immune recognition & responses to <i>B. anthracis</i>	VAMC-Boise
David Underhill	Inflammatory responses to <i>Francisella</i>	Institute for Systems Biology
George Happ	The ecology of <i>F. tularensis</i> in Alaska	University of Alaska
Carleen Collins	The <i>Yersinia pestis</i> insecticidal toxins	University of Washington
Becky L. Drees	Identification of candidate <i>Francisella</i> effector genes	University of Washington

c. The NWRBL will support NIAID-funded Biodefense and Emerging Infectious Diseases (EID) research

Federally sponsored Research in Washington State In the Northwest region, over a billion dollars in NIH funding is currently awarded. In Washington State alone, over \$144 million in NIAID-sponsored research is awarded. In addition to the WWAMI RCE projects listed above, the following research projects on category A, B & C priority pathogens are currently funded:

2004 Award amount	Grant #	Institution	PI	Title
351,000	AI059798-01	BENAROYA RES. INST. AT VIRGINIA MASON	Nepom, Gerald T	Mhc Tetramers For Epitopes Of <i>B Anthracis</i> Pa
109,620	AI057737-01	CHILDREN'S HOSPITAL AND REG MEDICAL CTR	Weissman, Scott J	Type 1 Fimbrial Variation In <i>E. Coli</i> 018 K1 H7 Virulence
5,599,999	AI062600-01	ID BIOMEDICAL CORP. OF WASHINGTON	Burt, David R	Development Of Proteosome-Adjuvanted Nasal Sars Vaccines
7,992,403	AI062567-01	ID BIOMEDICAL CORP. OF WASHINGTON	Lowell, George H	Development Of Protollin Plague Vaccine
451,841	AI041816-10	SEATTLE BIOMEDICAL RESEARCH INSTITUTE	Freitag, Nancy E	<i>Listeria</i> Virulence Gene Expression Within Host Cells
354,323	AI055651-01A1	SEATTLE BIOMEDICAL RESEARCH INSTITUTE	Freitag, Nancy E	Host-Pathogen Genetics Using <i>Listeria</i> And <i>Drosophila</i>
480,625	AI050506-03	SEATTLE BIOMEDICAL RESEARCH INSTITUTE	Parsons, Marilyn	The Plastid Of <i>Toxoplasma gondii</i>
338,082	AI047242-04	University of Washington	Cookson, Brad T	Cd4+ T Cells Responding To <i>Salmonella</i> Infection
48,928	AI054052-02	University of Washington	Crouch, Marielaure L	Role Of Iron Efflux In <i>Salmonella</i> Pathogenesis
341,100	AI039557-09	University of Washington	Fang, Ferric C	Nitric Oxide Cytotoxicity In Salmonellosis
379,000	AI050660-02	University of Washington	Fang, Ferric C	Dna Damage And Repair In <i>Salmonella</i> Pathogenesis
181,760	AI059503-01	University of Washington	Hughes, Kelly T	Flagellar Phase Variation In <i>Salmonella</i>
341,100	AI048622-03	University of Washington	Libby, Stephen J	The Sly A Regulon In <i>Salmonella</i> Pathogenesis
333,270	AI030479-15	University of Washington	Miller, Samuel I	Phop Regulon And <i>Salmonella</i> Virulence
301,136	AI048683-04	University of Washington	Miller, Samuel I	<i>Salmonella</i> Pathogenicity Island 2 Effector Proteins
293,600	AI044005-06	WASHINGTON STATE UNIVERSITY	Palmer, Guy H	Antigenic Variation In Rickettsial Transmission
300,724	AI058146-01	WASHINGTON STATE UNIVERSITY	Zhou, Zhaohui Sunny	Mechanism And Inhibition For Luxs: A Biodefense Target

NIAID-sponsored Research in Northwest United States Outside of Washington state, over \$21 million in NIAID-sponsored research is awarded in the Northwest region, including Alaska, Idaho, Montana, Wyoming, and Oregon. The following research projects on category A, B & C priority pathogens are currently awarded:

2004 Award amount	Grant #	Institution	PI	Title
157,480	AI061293-01	UNIVERSITY OF IDAHO	Arrizabalaga, Gustavo A	<i>Toxoplasma gondii</i> Egress
436,928	AI058536-01	LIGOCYTE PHARMACEUTICALS, INC.	Palecanda, Aiyappa M	Anthrax Vaccine Formulations Combining Pa/Spore Epitopes
212,250	AI044600-06	MONTANA STATE UNIVERSITY (BOZEMAN)	White, Michael W	Growth Regulation In <i>Toxoplasma gondii</i>
280,000	AI048390-04	MONTANA STATE UNIVERSITY (BOZEMAN)	White, Michael W	Control Of Dna Replication In Aids Pathogen <i>T. gondii</i> .
592,717	AI056286-01A1	MONTANA STATE UNIVERSITY (BOZEMAN)	Pascual, David W	Mucosal Vaccines For Plague
70,750	AI057021-02	MONTANA STATE UNIVERSITY (BOZEMAN)	Radke, Jay R	Study Of Permissive/Non-Permissive <i>T. gondii</i> Infections

245,000	AI059355-01	UNIVERSITY OF MONTANA	Nunberg, Jack H	Structure-Function Of Junin Virus Envelope Glycoproteins
377,500	AI019018-21	OREGON HEALTH & SCIENCE UNIVERSITY	Crosa, Jorge H	Iron Uptake As A Virulence Factor In Pathogenic Vibrios
353,415	AI022933-18	OREGON HEALTH & SCIENCE UNIVERSITY	Heffron, Fred L	Genetic Analysis Of <i>Salmonella</i> Virulence
377,500	AI059335-01	OREGON HEALTH & SCIENCE UNIVERSITY	Magun, Bruce E	Inflammatory Responses In The Toxicity Of Ricin
226,500	AI061527-01	OREGON HEALTH & SCIENCE UNIVERSITY	Nelson, Jay A	The Role Of Src Kinase In West Nile Virus Replication
302,000	AI061602-01	OREGON HEALTH & SCIENCE UNIVERSITY	Crosa, Jorge H	Iron Uptake And Virulence Of <i>Burkholderia pseudomallei</i>
279,552	AI021335-20	OREGON STATE UNIVERSITY	Hruby, Dennis E	Biology Of Vaccinia Virus Acylproteins
67,195	AI055569-02	OREGON STATE UNIVERSITY	Dreher, Theo W	Regulation Of West Nile Virus Gene Expression
275,569	AI060160-01	OREGON STATE UNIVERSITY	Hruby, Dennis E	Variola Virus G1I: An Antiviral Drug Target
227,500	AI047802-02	REED COLLEGE	Mellies, Jay L	Ler-Mediated Regulation Of EPEC Virulence Genes

Other Awards University of Washington Professor of Microbiology Michael Katze will be taking part in a multi-site NIH project “Molecular and Biological characterization of Spanish Flu” 1P01AI058113-01 (Proteomic Analysis Of The Innate Antiviral Response, AI056214-02, \$251,689). A University of Washington research team in the Department of Microbiology led by Michael Katze will collaborate with researchers from the Armed Forces Institute of Pathology and the Mount Sinai School of Medicine in New York to study the virus through a five-year, \$12.7 million grant from the National Institutes of Health as well as Scripps Research Institute and the Centers for Disease Control. The funding includes \$300,000 this year to develop a proper bio-containment facility for studying the pathology of the virus. The project will include animal model development as well as molecular biology and functional genomics research on the 1918 pandemic strain of influenza. Additionally, University of Washington Department of Immunology Chair Chris Wilson has recently been awarded an NIAID contract to investigate smallpox vaccine-associated myocarditis and polymorphisms in immune response genes (NO1-AI-40069, total Contract Amount \$7,778, 427). Smallpox vaccine is a key component of the national biodefense strategy, and the issue of smallpox vaccination and who should receive it is a subject of much debate in the public health community. Finally, NIH funding for infectious disease research is also granted to researchers at the UW through a number of other institutes, for example NHLBI, NIDDK, and NIGMS. These resources combine to create a nationally significant infrastructure of infectious disease centered on the University of Washington, providing an ideal site for the location of a regional biocontainment laboratory.

d. The NWRBL will contribute to institutional/regional/national biodefense research resources

The University of Washington School of Medicine is one of the nation’s foremost biomedical research institutions. For nearly 60 years, UW scientists have contributed to advancing scientific knowledge and saving lives. Researchers explore every aspect of health and disease, from the molecular mechanisms of gene action to population studies

of global illnesses. Their work has contributed to improved understanding of the cause of diseases and to better treatments and prevention of many disorders. UW School of Medicine has six faculty Nobel Prize laureates, 26 members of the National Academy of Sciences and 26 members of the Institute of Medicine. This school ranks first among public medical schools and second among all medical schools in federal research funding. In fiscal year 2003, it received \$488.5 million in National Institutes of Health research awards and \$165 million from private foundations, industry and other non-federal sources. The School of Medicine is closely affiliated with Children's Hospital and Regional Medical Center, Fred Hutchinson Cancer Research Center, VA Medical Centers: Seattle and American Lake, Washington; Boise Idaho, Seattle Cancer Care Alliance. In addition, UW School of Medicine provides medical care and training in a five state area (WWAMI) including Washington, Wyoming, Alaska, Montana and Idaho.

The NWRBL will attract more scientists into careers in biodefense and emerging infectious diseases. An active RBL will be a magnet for young researchers, particularly for young scientists already in school or working in the region. Through unique regional partnerships, outreach efforts will be expanded beyond the walls of the UW itself. The UW School of Medicine is unique in the nation in several ways that are important to the overall goals of the NIAID biodefense program. The School serves as the primary training center for medical personnel for an entire five-state region. Students do not simply come to UW to attend the School; to encourage students' ties to their local (mostly rural) areas, most students take their first year of medical school in residence at their home universities. Each state has a cadre of resident basic science faculty. In addition, professors from the UW also visit the first-year sites and teach various topics. All this means constant exchange of personnel and up-to-date information from the UW's research programs to the entire region.

The NWRBL will be in a unique position to exploit the WWAMI RCE's position into useful education and training, and do so without a major new investment of time or money. A large, experienced regional network of educators and researchers will be brought into play immediately upon startup of the NWRBL:

- The UW School of Public Health and Community Medicine which, through its Northwest Center for Public Health Practice (NWCPHP), works with states and communities on training for local public health officials.
- The WWAMI Program, which manages a decades-old, regional medical school in Washington, Wyoming, Alaska, Montana and Idaho.
- The WWAMI Area Health Education Center Network ("AHEC") which provides educational outreach efforts in the WWAMI region. Three WWAMI AHEC centers (Eastern Washington, Western Washington, Montana) have already received 2002-03 grant funding to train community-based providers in bioterrorism preparedness in partnership with the UW School of Public Health.
- The Biomedical Research Infrastructure Network (BRIN) initiative led by the UW School of Medicine: it is a consortium of biomedical researchers on campuses in the region.

In addition to these extended networks and centers, the University of Washington is home to a large number of Laboratories, Centers, Programs, and Projects. These organizations attract talented researchers as well as funding from the public and private sectors, and enhance the research environment of the University. A partial list of such entities that may benefit, and be benefited by, the NWRBL are:

- APEC Emerging Infections Network (APEC EINet)
(<http://depts.washington.edu/apecein/>)
- Applied Physics Laboratory (<http://www.apl.washington.edu/>)
- Center for Health Education and Research (CHER)
(<http://depts.washington.edu/cherweb/>)
- Center for Nanotechnology (<http://www.nano.washington.edu/index.asp>)
- UW Engineered Biomaterials (UWEB) (<http://www.uweb.engr.washington.edu/>)
- UW Genome Center (UWGC)
(<http://www.genome.washington.edu/UWGC/>)
- Global Trade, Transportation, and Logistics Studies (GTTL)
(<http://depts.washington.edu/gttl/>)
- Institute for Public Health Genetics (PHG) (<http://depts.washington.edu/phgen/>)
- Institute for Risk Analysis and Risk Communication (IRARC)
(<http://depts.washington.edu/irarc/>)
- International Training and Research in Emerging Infectious Diseases (ITREID)
(<http://depts.washington.edu/itreid/>)
- Molecular Microbiology in Laboratory Medicine
(<http://depts.washington.edu/molmicdx/>)
- National ESCA Surface Analysis Center for Biomedical Problems (NESAC/BIO)
(<http://www.nb.engr.washington.edu/>)
- Northwest Center for Occupational Health and Safety
(<http://depts.washington.edu/ehce/NWcenter/>)
- Northwest Center for Public Health Practice
(<http://healthlinks.washington.edu/nwcphp/>)
- Occupational Epidemiology and Health Outcomes Program
(<http://depts.washington.edu/occepi/>)
- Washington Technology Center (<http://www.watechcenter.org/>)
- WWAMI Rural Health Research Center (RHRC)
<http://www.fammed.washington.edu/wwamirhrc/>

The Scientific Oversight Committee will take an active role in using this extensive network to identify and prioritize research to take place at the NWRBL. By a combination of direct solicitation, letters to departmental heads, announcements in periodicals and web presence, individuals will be contacted who might benefit by using the biocontainment facilities at the NWRBL. Through an application process whereby proposals will be accepted and reviewed quarterly, approximately 15-20% of the laboratory capacity will be dedicated to these shorter-term occupants on an ongoing basis. Recommendations of the Committee will be forwarded by its Director Sam Miller to PI Paul Ramsey. The user of this type of mechanism is anticipated to be a researcher whose project has expanded to include priority pathogens, or for whom key experiments require this special level of containment. The Committee will develop specific policies and cost structures associated with these research activities, in coordination with the overall administration of the facility at the UW campus.

e. The NWRBL will execute a national emergency response plan in the event of a bioterrorism attack or infectious disease outbreak The NW Regional Biocontainment Laboratory will be sited in an environment which is well-connected to regional and national networks. Both in laboratory collaboration and in teaching, the UW already has an extensive working relationship with the six northwestern states (WA, OR, ID, MT, WY, AK) that will serve as the RBL's framework for information dissemination, training and laboratory emergency response coordination. In addition, the WWAMI RCE under Sam

Miller is already well integrated with federal response plans in the region and nationally. The USPHS Regional Health Administrator for Region X, Capt. Patrick O'Carroll is the most active Affiliate Associate Professor in the School of Public Health and Community Medicine. He is now responsible for overall coordination of the public health response to bioterrorism in the region. Dr. O'Carroll previously set up CDC's Health Alert Network (HAN) to coordinate emergency communication between the federal government and state and local health agencies in the country. Before moving to the Region X position in 2003, he spent four of the last six years as a full-time CDC assignee to UW's NWCPHP to work specifically in the northwest region and to help set up the pioneering public health informatics research and training program at UW (<http://phig.washington.edu/>). Dr. Mark Oberle, the Associate Dean for Public Health Practice at the UW School of Public Health, coordinates collaborations with state and local institutions and organizations for the WWAMI RCE in addition to the UW School of Public Health. As an example of the UW collaboration with federal, state and local partners, UW has hosted Washington State's pharmaceutical stockpile dispensing exercise, the first such state drill in the country after the anthrax epidemic. At the drill held on the UW campus, 269 "patients" exposed to anthrax were registered, evaluated, and treated using supplies from the National Pharmaceutical Stockpile. The exercise has resulted in two publications in press with UW, state and local emergency response authors.

The Northwest Center for Public Health Practice (UW/NWCPHP) has a network of six state public health training coordinators that meet quarterly and convened the first joint meeting with the six states' HAN directors and the 6 state bioterrorism preparedness coordinators. In addition, the UW/NWCPHP under the direction of Prof. Jon Counts, former director of the Washington State Public Health Laboratory, has a project with the public health laboratory directors in the six states to improve infectious disease laboratory practice. This group began meeting in 2002 and communicates via a newsletter and listserve and comprises the coordinators of CDC's Laboratory Response Network in the region for integration of laboratory surge capacity in managing laboratory specimens. The NWRBL Scientific Oversight Committee will interact with this group to determine which facilities at the RBL would be useful to Public Health Laboratories for surge capacity or specialized testing such as molecular characterization of strains, which include DNA sequencing, mass spectrometry protein characterization, and the genomic evaluation of strain similarity. Romesh Gautam, Ph.D., the DOH director of the Public Health Laboratory of the Washington State Department of Health, will be the point of contact for the NWRBL with this agency on an ongoing basis and in the event of a public health crisis. Although primarily a research facility, the NWRBL could enlarge the State's capacity to protect the public by handling overflow needs for analysis of biological agents.

At the local level in Seattle-King County, Dr. Jeff Duchin is both the director of the infectious disease control program at the Seattle King County Public Health responsible for bioterrorism response and is an Assistant Professor at UW in both Medicine (Infectious Diseases) and Epidemiology. Dr Duchin communicates almost daily with Infectious Disease clinicians throughout the state on issues of public health interest and he is a personal friend of the Director of the WWAMI RCE (Miller).

After the submission of this application, Sam Miller will utilize the next quarterly meeting of the six-state network to evaluate other potential partners, and establish a plan to define a regional role for the NWRBL to assist in the response. The WWAMI RCE Directors regularly attend the quarterly meetings of the six state networks, and they will keep that group informed of the RBL research and infrastructure capability. This will also be an opportunity to work with this group to define in advance what emergency demands might be placed on the laboratory. In the event of a biodefense or emerging

infectious disease emergency, the members of the NWRBL Scientific Oversight Committee will be available to assist Dr. Patrick O'Carroll and other federal and state officials to expedite planning as necessary. Since management of the NWRBL as a shared resource is expected to involve limited tenancies by scientists, space availability in the advent of an emergency is expected to be very responsive. More immediately, NWRBL key personnel will be available on a 24-hour basis by beeper and cell phone to assist in coordinating the response.

f. The NWRBL will establish and enact a Community Relations Plan

Approach to Outreach

The goal of the community relations plan is to proactively create positive relations concerning this grant within the research community, the University community and surrounding residential/commercial communities, and the general public throughout the application process, construction and operation of the facility. The community outreach plan will be front loaded with the majority of the activities occurring during the first phase of the project. The second two phases will include the same activities as described in the first phase with the exclusion of the letters of support from public officials. Those phases include 1) application process (December 2004 to June 2005) 2) design of the facility (Summer 2005 to Summer 2007), and 3) Construction of the facility (beginning Summer 2007) with occupancy occurring in 2009/2010.

Public Involvement

The campus and community will be informed and advised of the projects progress during each of the three major phases of project from application through design and construction. Each phase will begin with information being shared with the stakeholders and opportunities for input and information sharing.

Phase 1: Application Process, December 2004 to June 2005

Seek letters of support from local, regional and state leadership once grant has been submitted

The elected leadership of the local, regional and state governing bodies will be informed of the grant application in December 2004 as the application is being submitted. The state's leadership has always been supportive of the University's role in research and its positive impact on the local, state and regional economy. The letters will be complete and received by NIH no later than January 12, 2005. While we hope to get a letter of support from the Governor, because of the recounting of ballots, it may not be possible to get a letter of support because we will not know who the governor elect is until mid-January. Letters of support will come from:

- United States Senator Patty Murray
- United States Senator Maria Cantwell
- City of Seattle Mayor, Greg Nickels
- Governor-elect

Community Approval of the Campus Master Plan (CMP) included development approval for site 45S

The potential development site for the Regional Bio-containment Facility is site 45S. This site (along with some 60 others) were approved for future development by the

community, Seattle City Council, Mayor and the Board of Regents in January 2003 after a four year process which ended in the approval of the Campus Master Plan.

The Campus Master Plan is the written document that guides the physical development of the Seattle campus. The community outreach plan followed for the development and approval of the CMP can be found in Chapter VIII and Appendix D of the CMP which can be viewed at the following web-address:

http://www.washington.edu/community/cmp/Plan_Background.html.

The process the University followed to seek final approval for the University's physical development plan is outlined in the 1998 City University Agreement that can be viewed at <http://www.washington.edu/community/cuagree.html>. The process encourages open, active, and meaningful participation by both the University community of faculty, staff and students as well as the community groups and residents that live around the University. During the four years it took to approve this plan, the Campus Master Plan staff held or attended 137 meetings during which time information about the plan was shared and comments and concerns were addressed. Before the Plan could be approved by the Board of Regents, the nine members of the Seattle City Council had to approve the legislation and send it to the Mayor for his signature. Because of the active participation of the City leadership, the future development of the site chosen for the bio-containment lab has already been approved.

Community Outreach Plan for Bio-containment Facility builds upon Community Approval of Campus Master Plan

The community outreach plan for the approval of the CMP was extensive and comprehensive. The site that will potentially house the bio-containment lab has already been approved for development of an academic facility so there will be no additional input needed for site approval.

The public outreach process will focus on educating the local, regional and state leaders on the importance of having a bio-containment facility in the region and getting their support for one at the University of Washington.

The University's presence in the community extends far beyond its role as an academic institution. It is a nationally recognized center for research projects and medical services, a hub for cultural resources and events, and a recreational center for the community and the region. During the last fiscal year, the University received over \$1 billion dollars in research funds. Diverse audiences have a vested interest in the future of the University. The University will actively solicit and include the participation and input from the following individuals, groups, and organizations in addition to any others that wish to participate:

- Campus community (Students, Faculty, Staff, Board of Regents)
- City of Seattle
- King County Government
- Biomedical associations and groups
- General Public
- Adjacent neighborhoods, communities, and businesses

Community Input for Bio-containment laboratory starts with the City University Community Advisory Committee (CUCAC)

CUCAC has been the University's Citizen's Advisory Committee for 28 years. It was created by the Seattle City Council in 1977 to advise the University and the City on the orderly development of the Seattle campus. The City and the University recognized that the impact of the University on its neighborhood is positive in many ways, but at the same time they also realized that the University's mission may have adverse impacts on the City and surrounding communities. With the creation of CUCAC, the University and the City institutionalized the residential and business communities' voice in its orderly development of buildings and programs on campus. A discussion of the program, the grant application and the development site will be on the committees agenda for January through April of 2005.

CUCAC is comprised of 16 individuals who represent 12 neighborhood organizations that are in close proximity to the University. The other four representatives represent the UW faculty, staff, and students along with one UW at-large representative.

The community organizations are listed below:

- Eastlake Community Council
- Greater University District Chamber of Commerce
- Laurelhurst Community Club
- Montlake Community Club
- Portage Bay/Roanoke Community Council
- Ravenna-Bryant Community Association
- Ravenna Springs Community Group
- Roosevelt Neighbor's Alliance
- Roosevelt Neighborhood Association
- University District Community Council
- University Park Community Club
- Wallingford Community Council
- University Faculty, Staff, Students and At-Large Members

Business Organizations around the University will be an integral part of the Outreach Plan

There are several organizations within the business districts that border the University that will be consulted in early 2005 once the grant is submitted. Representatives from the grant application team will be on the their monthly meeting agendas. These groups represent the businesses and neighborhood groups in the Greater University and North Capitol Hill and Eastlake areas including:

- Northeast District Council
- Greater University District Chamber of Commerce
- The AVE Group

Keeping Major Stakeholders Informed will be done in several ways

The University will take the information and questions received from the many meetings detailed above to produce communications materials. These materials will be used throughout the application, design/construction and facility operation process to keep stakeholders informed of its progress, issues, and developments. Those materials will include:

- **Project Overview Brochure** – discusses the application process and timeline, the design and construction timeline and facility operation issues. It will be distributed in response to general inquiries.
- **Newsletters** - distributed as an article in University Week and/or an insert into U Week and as a self-mailer to the stakeholders prior to public meetings in each phase of the project or as needed.
- **Fact Sheets** – distributed at public meetings and in response to inquiries as needed.
- **Frequently Asked Questions (FAQ's)** - distributed at public meetings and in response to inquiries as needed.
- **Regional Bio-containment Laboratory Website** - The University will create a website that will provide general information, project overview brochure, updates, fact sheets, documents, and FAQ's, news articles, and information on how to submit comments
- **Regional Bio-containment Database**

The University will develop and maintain a database of stakeholders, organizations and individuals interested in learning about the project and participating as it is developed. The database will initially be assembled using several existing campus and community mailing lists including various University committee and council rosters, University's SEPA Mailing List, Greater University District Chamber of Commerce, City University Community Advisory Committee (CUCAC), and the NE District Neighborhood Council. State, City, and County agencies and local elected officials will also be included in the database as well as the Single Point of Contact. Throughout the project, names will be added to the database from open houses, through comment submissions, or through requests made via the Regional Bio-Containment Grant web-site and e-mail address.

- **Regional Bio-containment E-mail address**

The University will create an e-mail account for individuals to request information or share comments or concerns

- **Regional Bio-containment office address that interested parties can send correspondence:**

The University will create a mailing address to which individuals can send correspondence to request information or share comments or concerns

- **Media** -Print and broadcast media will be used to build general community awareness, disseminate information, and encourage public participation in the three phases of development of the facility through media releases, meeting notification advertisements, and community calendars. The Health Sciences News and Information Services will contact the science writers from the major papers (Times and PI) and conduct "Research Forums" to better educate the media about the research that will be done with the creation of a Regional Bio-containment Laboratory. Media markets and publications will include campus publications, community newsletters, neighborhood newspapers, and local/regional/national publications such as:

- University Herald
- Capitol Hill Times
- Madison Park Times
- North Central Outlook
- Seattle Press
- The Daily
- Seattle Times
- Seattle PI