CENTER FOR ADVANCING MICROBIAL RISK ASSESSMENT

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DHS-EPA Cooperative Center of Excellence on the Methods and Science to Conduct n Microbial Risk Assessment in Support of Homeland Security Objectives. 2004-STAR-P1

Project Title: The Center for Advancing Microbial Risk Assessment (CAMRA)

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Lead Institution: Michigan State University

Participating Institutions: Carnegie Mellon University (CMU), Drexel University, Michigan State University (MSU) , Northern Arizona University (NAU), University of Arizona(UA), University of California at Berkeley (UCB), University of Michigan (UM).

Center Budget: $10,000,000

Project Period: May 15, 2005-May 14, 2010

Project Summary: CAMRA is a consortium of scientists who have extensive expertise in quantitative microbial risk assessment (MRA) methods, biosecurity and infectious disease transmission through environmental exposures. CAMRA has two main goals. The first is a technical mission to have developed critically reviewed and interpreted sets of models, tools and information that will be used in a credible risk assessment framework to reduce or eliminate health impacts from deliberate use of biological agents of concern (BAC) as bioterrorists agents in the indoor and outdoor environment. The second mission is to build a national network for MRA for knowledge management, learning and transfer, for the community of scientists, and students via educational programs and community of professionals in the field and in our communities. There are five major research projects which will define the goals and activities of CAMRA. Each project goal has been developed through collaborative efforts of scientists and will be integrated via a management structure that facilitates interaction. They address exposure, methods and models; dose-response; population outcomes; risk frameworks; knowledge management, transfer and learning. Overall these projects will focus on assessments, lessons learned, new science and research, databases, tools and methods and finally knowledge building for learning and communication purposes.

Expected Results or Benefits: We anticipate that CAMRA will produce a suite of outcomes for government officials and first responders as well as the research, education, and professional communities. We will provide documentation on the sensitivity and specificity of risk assessment methods and their ability to address levels of safety. A toolbox with validated surrogates for BAC will be produced. The fate and transport of bioterrorist agents in water distribution systems, air and buildings will be evaluated. Models for characterizing exposure via aerosols and the indoor environment that are validated with real-world data where available. We will produce an inventory of critically analysed dose-response relationships for Category A agents and mechanistic dose-response models (based on physiological-based, dose-response). Stochastic and deterministic dynamic disease transmission population models (accounting for heterogeneity in exposure), models for assessing controls (eg. vaccines, quarantines, decontamination, clinically intervention and treatment) .

Supplemental Keywords: biological agents, bioterrorism, quantitative microbial risk assessment, pathogens, dose-response, exposure assessment, risk management.

DHS-EPA Cooperative Center of Excellence on the Methods and Science to Conduct Microbial Risk Assessment in Support of Homeland Security Objectives. 2004-STAR-P1
Project I Title: Exposure: Detection, Fate and Transport of Agents

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Project Summary

The goal of this project is to improve our ability to quantify exposure to biological agents of concern (Category A and B agents) in drinking water systems and indoor air environments. Because BAC agents are too hazardous to work with in the environments we wish to study, it will be necessary to develop surrogates so that assessments can be made under real world conditions. This project draws together several groups with extensive experience in the detection, transport and fate of BAC in aerosols, water and fomites, and transmission dynamics of Category A and B agents in the environment. This goal will be met through a series of specific sub-project objectives Including: 1) Development of BAC surrogates 2) Validation of detection methods (Assessment of best methods; Surrogate methods identification; Sample needs for risk models; Gene sequences as a tool in risk assessment); 3) Modeling BAC in water systems (model development and design; Field studies utilizing the Water Village); 4) Survival and transfer via fomite surfaces; 5) Development and validation of a discrete-time Markov chain model for Airborne BAC within a room. 6) Evaluation of particle fate and transport in a room; 6) Model for resuspension of particles and 7) Determination particle size distribution in aerosols.

EXPECTED RESULTS AND BENEFITS: It is anticipated that this Project will result in an improvement in the ability to determine the exposure to BAC during contamination events in the indoor environment (air and surfaces) and via water. Thus an assessment of the detection methods and better exposure estimates will inform the risk framework and the management strategies that are needed including clean up targets defined by “safety” levels.

Supplemental Keywords: Biological Agents, Surrogates, Survival, aerosols, Water, Transport, Exposure.

DHS-EPA Cooperative Center of Excellence on the Methods and Science to Conduct Microbial Risk Assessment in Support of Homeland Security Objectives. 2004-STAR-P1

Project II Title: Infectious Disease Models for Assessing Microbial Risks and Developing Control Strategies.

Investigators: Joseph N.S. Eisenberg and James Koopman; Collaborating Investigators: Alan Hubbard, Arthur Reingold (UC Berkeley).
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Institutions : Univ. California Berkeley, University of Michigan.

Project Summary: I) Objectives: The recent increase in the concern of bioterrorism has expanded the needs of microbial risk assessment. We propose to develop a methodology that provides explicit links between the models of environmental exposure and models of the disease process, focusing on how heterogeneity will impact risk. This methodology will be used to integrate environmental and dose-response data and to aid in: a) early detection of outbreaks; b) planning for both short- and long-term control efforts, and c) setting research agendas. To this end, we propose the following three specific aims: 1) To develop appropriate transmission models that are dynamic and provide spatially explicit details of infection spread through populations; 2) To use existing data sets to identify parameters of interest including secondary transmission rates, contact patterns, and dose response functions; and 3) To use the models developed in the previous objectives to analyze different outbreak scenarios associated with local contamination, to examine the efficacy of local control actions at different environmental points or within different population groups, and to develop and evaluate sampling and analysis methods that can be used under the emergency conditions of a bioterrorist related outbreak, as a guide for resource allocation.
II) Approach: In Aim 1 we will construct models of transmission through water and through droplet spread involving direct contact, fomites, and surfaces at environmental sites. These models will include descriptions of the pathogen fate and transport processes within the environment. We also plan to develop approaches for identifying values for parameters used in a given model. In Aim 2, therefore, we plan to first create a database of information important to parameterizing and identifying models, and second to examine a variety of statistical techniques that address the problems associated with highly parameterized nonlinear models. In Aim 3 we plan to develop scenario models for evaluating bioterrorist control strategies, analyze strategies that can be used in emergency situations, and propose ways to use environmental measurements to guide control actions

EXPECTED RESULTS OR BENEFITS

This research will contribute essential elements to control of a bioterrorist disease outbreak related to infections and contribute the essential tools for analyzing bioterrorist emergency situations involving transmissible agents.

Supplemental Keywords: microbial risk assessment, pathogens, bioterrorism, decision-making, mathematics, modeling.

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Project III Title: Dose Response Assessment

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Michigan State University, East Lansing, MI

Project Summary:

The objectives of the proposed work are to:

1) To determine the applicability of exponential, beta-Poisson and other previously used dose-response models to the Category A bioterrorist agents via the oral, inhalation and dermal routes.
2) To assess the validity of animal to human extrapolation of dose-response.
3) To assess the influence of modifying factors (e.g., host age) on dose-response.
4) To develop a new class of physiologically-based dose-response functions and to test their applicability on bioterrorist agents.
5) To conduct animal studies which will help inform the development of the above dose-response models.

We will review the archival literature and the "gray" literature for data sources to inform dose-response models, and subject that data to a systematic quality screen. We will fit candidate dose-response models to each data set, test strain and host differences, and assess the impact of other variables (such as host age). We will test the dose-response fits to available data on outbreak or endemic cases (where such information is available). We will use information on the *in vivo* fate, transport, and dynamics, of pathogens in humans and non-human hosts to develop models that start with the ingested/inhaled/dermal dose, predict the dose at the point of colonization and the extent of reproduction, and use these predictions in a dose-response relationship for outcome. It is our hypothesis that such models may be useful in assessing factors associated with different host-sensitivities, effect of concomitant exposures to other materials, and interspecies extrapolations. We will conduct animal studies to assess the infectivity of certain select pathogens where there appear to be significant data gaps. These studies will inform the development of both "classical" and physiologically based dose-response models.

EXPECTED RESULTS OR BENEFITS

This project will produce a reference set of critically reviewed dose-response relationships for Category A agents. By compiling dose-response relationships in various hosts and for various strains, in conjunction with information from other projects in CAMRA, we will be able to ascertain the inter-(microbe)species heterogeneity in infectivity, and determine whether there are discernable genetic markers which may be correlated to such differences. This may facilitate an assessment of the potential for further alterations in a strain to change potency.

Supplemental Keywords: Dose-response, statistics, infectivity, select agents, inhalation, ingestion, dermal exposure, interspecies extrapolation, physiological models
Research Category: DHS-EPA Cooperative Center of Excellence on the Methods and Science to Conduct Microbial Risk Assessments in Support of Homeland Security Objectives
Sorting Code: 2004-START-P1

DHS-EPA Cooperative Center of Excellence on the Methods and Science to Conduct Microbial Risk Assessment in Support of Homeland Security Objectives. 2004-STAR-P1

Project IV Title: The Assessment-analysis Interface

Investigators: Patrick Gurian, Department of Civil, Architectural, and Environmental Engineering, Drexel University; Elizabeth Casman, Department of Engineering and Public Policy, Carnegie Mellon University; Mitchell Small, Department of Civil and Environmental Engineering, Carnegie Mellon University; Julie Downs, Department of Social and Decision Sciences, Carnegie Mellon University.
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Institutions: Drexel University, Philadelphia, Pennsylvania
Carnegie Mellon University, Pittsburgh, Pennsylvania

Project Period: May 15, 2005-May 14, 2010

Project Summary

Objectives:

This project will link the technical research on bio-threats conducted in other CAMRA projects with the societal goal of managing the risk of bioterrorism through two related research efforts. The first effort will use techniques from decision analysis to prioritize research efforts based on their ability to improve the response to bioterrorism incidents. The second effort will identify and begin to address critical issues of public perception that have the potential to influence the public's compliance with response and mitigation plans.

Approach:

An integrated model of bio-threat fate and transport, dose-response, secondary transmission, and mitigation actions will be developed. The ability of alternative research efforts to reduce uncertainties in different inputs to this integrated model will be assessed. Value-of-information calculations will be conducted to identify the research strategies most likely to yield knowledge that improves the response to bioterrorism incidents. Risk communication priorities will be identified using the "mental models" approach. This begins with an assessment of expert knowledge and representation of this knowledge in an influence diagram. Baseline public knowledge and attitudes are assessed by semi-structured interviews and surveys. The lay knowledge is then compared to the expert model and key misconceptions and information deficiencies are identified. Future risk communication efforts may then be directed towards addressing these key deficiencies.

EXPECTED RESULTS OR BENEFITS:

This project will identify promising research strategies with the potential to improve the societal management of bioterrorism risk. In addition, it will develop a list of risk communication priorities for both pre-event public education and post-event response plans. This project will link together Projects I-III through the development of an integrated model and will identify critical information for inclusion in the knowledge and information repositories of Project V.

Supplemental Keywords: Risk management, decision-making, psychology, statistics
Research Category: DHS-EPA Cooperative Center of Excellence on the Methods and Science to Conduct Microbial Risk Assessment in Support of Homeland Security Objectives
Sorting Code Number: 2004-STAR-P1

DHS-EPA Cooperative Center of Excellence on the Methods and Science to Conduct Microbial Risk Assessment in Support of Homeland Security Objectives. 2004-STAR-P1

Project V. Title: Knowledge Management, Transfer, and Learning

Investigators: Rosina Weber. Co-PIs: H. Han, M. Atwood, C. Haas, Drexel University
URL: http://www.pages.drexel.edu/~rw37/projects/ckmmra.html: Dr. Ewen Todd,
Email: rweber@cis.drexel.edu; toddewen@cvm.msu.edu
Institutions: Drexel University 3141 Chestnut street Philadelphia, PA 19104; Center for Food Safety and Toxicology, Michigan State University.

Project Period: Starting on April 1st, 2005 and ending on March 31st, 2010

Project Summary:
It is the overall objective of this project to investigate and implement effective and efficient methods to enhance the understanding of microbial risk assessment (MRA) as a body of knowledge. For this purpose, we focus on education and collaboration in combination with technological methods to promote knowledge leveraging, management, transfer and learning among members of the Center for Advancing Microbial Risk Assessment (CAMRA). These are the objectives, approaches, and expected results from this project:
1. Build an online collaborative repository. This will be a knowledge repository because it will use learning units represented as a knowledge formalism. Learning units will specify the task where they can be reused. The knowledge repository will promote knowledge leveraging and sharing among CAMRA's members.
2. Reason with learning units for knowledge discovery. The learning units are amenable to automated reasoning. Reasoning methods can leverage MRA's knowledge.
3. Build a data warehouse from data linked to the learning units. Additional knowledge discovery methods can be applied over the data warehouse. The data warehouse will be publicly available.
4. Develop targeted educational programs

EXPECTED RESULTS OR BENEFITS: Approaches will achieve development of an intellectual knowledge base and a CAMRA website and other dissemination means. This will support the community of practice for risk assessment principals. Produce productive and effective knowledge sharing. Finally research data will be used to develop a framework for different community of users for MRA for BAC and recommendations for policy to reduce the risk of transmission of select and other agents to populations in the U.S.. Educational programs will produce core graduate level courses for MRA, on-line learning tools and workshops to support collaborations and common aims.

Supplemental Keywords: microbial risk assessment, repository, knowledge management, learning tools, educational programs.

RESEARCH PLAN FOR THE CENTER FOR ADVANCING MICROBIAL RISK ASSESSMENT (CAMRA)

The Center for Advancing Microbial Risk Assessment (CAMRA) is a consortium of scientists in microbiology, medicine, infectious disease, veterinary medicine, engineering, food and water safety, environmental science, ecology and evolutionary biology and computational intelligence who have expertise in quantitative microbial risk assessment (MRA) methods, biosecurity and infectious disease transmission through environmental exposures. CAMRA is comprised of seven University teams (Figure E1)

The Center Co-Directors Dr. Rose (MSU) and Dr. Haas (Drexel) as well as the principal investigators all have a long history (as much as 20 years) of working together on advancing the data, information and knowledge on microbial risk assessment and infectious disease. CAMRA represents a crescendo of those efforts.

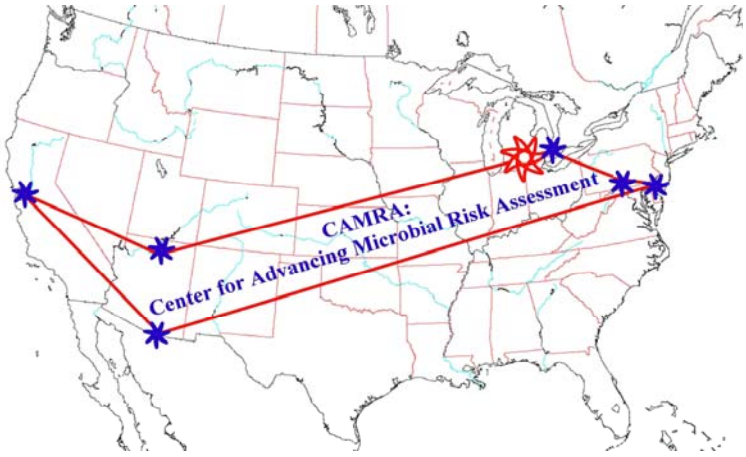


Figure 1. CAMRA participants: Carnegie Mellon University (CMU), Drexel University, Michigan State University (MSU) , Northern Arizona University (NAU), University of Arizona (UA), University of California at Berkeley (UCB), University of Michigan (UM).

The Mission of CAMRA

CAMRA has twin missions. The first is a technical mission to have developed critically reviewed and interpreted sets of models, tools and information that will be used in a credible risk assessment framework to reduce or eliminate health impacts from deliberate use of biological agents of concern (BAC) as bioterrorists agents in the indoor and outdoor environment. The second mission is to build a national network for MRA for knowledge management, learning and transfer, for the community of scientists, community of students via educational programs and community of professionals in the field and in our communities.

The Vision and Rationale of CAMRA

Microbial risk assessment has been developed and used during the past 20 years to address concerns associated with the quality of our water and food and directly waterborne and foodborne disease transmission (Haas, Rose, and Gerba, 1999; Eisenberg et al., 2002 [see cv of principal investigators). These risk assessments have assisted the EPA (Macler and Regli, 1993) and USDSA/FDA (Buchanan and Whiting, 1996) in developing regulatory policy and implementing management plans. The recent increase in the concern of bioterrorism has expanded the needs of microbial risk assessment. In the context of bioterrorism four important objectives are: 1) To assess the damage/risk (impact and spread) of different plausible bioterrorism scenarios in order to aid in policy and decision-making for preparedness and response; 2) To improve effectiveness and enhance safety of the response in the event of a bio-terrorist attack, by improving public health surveillance of environmental exposure, infection,

and disease as well as infection control actions like contact tracing, early detection of infections, treatment, isolation, quarantine, chemoprophylaxis, vaccination, and decontamination; 3) To guide research into the development of tools and biomonitoring strategies for infectious disease BAC detection in environmental samples, that will best help infection control during bioterrorist episodes (eg. disinfection); and 4) To develop prevention and monitoring strategies for public health protection in general from BAC.

There is a heightened concern for future bioterrorist events since the fall 2001 anthrax incident and it has become clear that there is a lack of knowledge with respect to certain important questions regarding exposure to infectious BAC, particularly those that can be transmitted by inhalation. Notably, the stipulation of "safe" (or unsafe) levels, or cleanup goals following a contamination event have not been well defined using science-based and risk-based methods. The question "How Clean is Clean" has not yet been answered in the concrete with respect to bioterrorist agents (Raber *et al.*, 2001) and in fact the same is true for many other environmental BAC.

The development of a microbial risk framework relevant to bioterroism issues requires focused research on some important properties of outbreaks and disease transmission that would arise from a bioterrorist incident. To accurately characterize the risk will require models that are dynamic, that focus specifically on the key BAC, can account for the heterogeneous nature of the disease process, and can clearly link exposure to health effects. The **vision of CAMRA** is to provide explicit links between the models of environmental exposure and models of the disease process, focusing on how heterogeneity will impact risk, evaluation of uncertainty and advancement of the knowledge base for MRA.

The Research Objectives of CAMRA

There are five major research projects which will define the goals and activities of CAMRA. Each project goal has been developed through collaborative efforts of scientists with more than one University involved. Overall these projects will focus on assessments, lessons learned, new science and research, databases, tools and methods and finally knowledge building for learning and communication purposes.

- **Project I. Exposure: Detection, Fate and Transport of Biological Agents of Concern (BAC).** [Lead: Dr. Charles Gerba UA] The overall goal of this project is to improve the ability to determine the exposure to BAC during contamination events in the indoor environment (air and surfaces) and via water. Thus an assessment of the detection methods and better exposure estimates will inform the risk framework and the management strategies that are needed including clean up targets defined by "safety" levels.

Specific Objectives:

Development of new BAC surrogates for application in methods assessment and transport and fate modeling efforts. (Gerba, UA; Hashsham, MSU; Keim, NAU)
Validation of detection methods for microbial risk assessment. (Hashsham & Rose, MSU; Keim, NAU)
Development of fate and transport models for BAC on fomites (surfaces). (Gerba & Choi, UA)
Development of fate and transport models for BAC in water systems. (Gerba & Choi, UA; Haas, Drexel)

Development and validation of a discrete-time Markov chain model for Airborne BAC within a room. (Nicas, UCB; Haas, Drexel)
Measure the re-suspension of particle-associated BAC in a test room or chamber (Nicas, UCB)
Determine the particle size distribution of respiratory aerosol (Nicas, UCB)

- **Project II. Infectious Disease Models for Assessing Microbial Risks and Developing Control Strategies.** [Lead: Dr. Joseph Eisenberg, UCB] The overall goal of this project is to develop a methodology that provides explicit links between the models of environmental exposure and models of the disease process, focusing on how heterogeneity will impact risk. This methodology will be used to integrate environmental and dose-response data and to aid in: a) early detection of outbreaks; b) planning for both short- and long-term control efforts, and c) setting research agendas.

Specific Objectives

Developing transmission models (Eisenberg, UCB; Koopman, UM)
Model parameterization and identifiability (Eisenberg, UCB; Koopman, UM)
Modeling Outbreaks and developing control strategies (Eisenberg, UCB; Koopman, UM; Bolin, MSU; Keim, NAU)

- **Project III Dose-response Modeling and Applications**. [Lead Dr. Charles Haas, Drexel] The overall goal of this project is to comprehensively review and analyze dose response relationships for BAC and develop mechanistic models from animal studies. This will inform the population modeling, and facilitate decision making (emergency response and monitoring) with comprehensive risk-based assessment of detection technology and cleanup alternatives.

Specific Objectives

Development of dose-response relationships. (Haas, Drexel)
Development of Physiologically based dose-response models. (Haas, Drexel; Bolin, MSU).

- **Project IV. Assessment-Analysis Interface.** [Lead: Dr. Patrick Gurian, Drexel] The goal of this project is to use analytical approaches from statistics, decision analysis, and psychology to produce a prioritization of data and information needs and to identify, and begin to address, social factors that can significantly influence risk. By focusing research efforts on productive lines of inquiry, this project has the potential to greatly improve the practical usefulness of the results derived from the proposed research center.

Specific Objectives

Identification of scenarios and modeling tools (Gurian, Drexel; Casman & Small, CMU)
Public perception of Bio-threat risks (Casman, CMU)
Development of probabilistic descriptions of uncertainty and relatedness (Gurian, Drexel; Casman, CMU; Todd, MSU)
Value-of-information calculations (Gurian, Drexel; Casman, CMU)
Implementation of results and iterative refinement of calculations. (Gurian, Drexel; Casman, CMU)

- **Project V. Knowledge Management, Learning and Discovery.** [Leads: Dr. Rosina Weber & Dr. Ewen Todd] The overall goal is to provide effective and efficient technological support for group collaborations, that results in a knowledge repository linked to a data repository, where knowledge can be discovered and leveraged, helping to advance different fields of study including programs in higher education and outreach to the community of professionals.

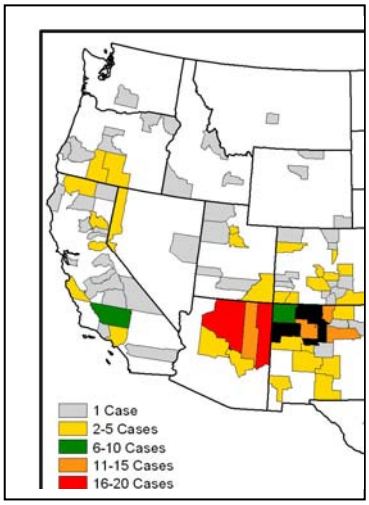
Specific Objectives

Build an online repository based on evolving learning unit. (Weber & Haas, Drexel; Rose, MSU)
Reason with learning units for knowledge discovery. (Weber, Drexel & Exec. Steering Committee)
Build data ware house from data linked to the learning units (Weber & Gurian, Drexel; & Exec. Steering and Integration Team ESI)
Produce targeted educational programs: (graduate level curriculum, online learning tools, workshop series (Todd, Rose, MSU & ESI)

Needs, Expected Benefits and Outcomes

There are a number of disease causing microorganisms which have characteristics that would facilitate their use as agents for terrorist type of activities or as biological weapons [ability to be produced in large amounts, purified, stored and delivered to large populations] and a number of biological agents of concern (BAC) have been weaponized particularly for aerosol dispersion as inhalation can often cause more severe outcomes. Historically, there are records of poisoning of the water supply as early as the 6th Century B.C., use of plague in 1348 by the Mongols in the city of Caffa and use of Small pox in the French & Indian War. In our more recent history, in 1984 the Rajneeshee Cult contaminated salad bars with *S. typhimurium* (where 750+ individuals became ill) in an attempt to influence an election outcome in Oregon (Torok et al., 1997) and finally the experience of the Anthrax letters contamination event of 2001 is still quite fresh in our minds (Jernigan et al. 2001). In fact, anthrax has been reportedly used more often as a real threat or implicated in a hoax than any other BAC.

Figure 2. Human Plague



New and emerging BAC and outbreaks of familiar diseases are constantly in the news. An anthrax outbreak killing 1500 animals in two conservation areas next to one of Zimbabwe's largest game parks, was the first and largest event ever reported in that part of the world in September (AP From correspondents in Harare, September 27, 2004). The Cruise ship outbreaks of norovirus are a significant concern for the tourism industry. Human cases of plague continue to be reported in the US (www.cdc.gov/ncidod/dvbid/plague/ plagwest.htm Figure E2).

The rapid global spread of SARS is a prime example of an emerging virus, with the potential to kill, that was found to thwart efforts of traditional infection control (Wu, 2003; WHO, 2003) and required genetic approaches to help identify the threat. **Thus there is a need to study and distinguish between intentional and naturally-occurring outbreaks and address these emerging threats.** The prevention and control of infectious diseases requires an understanding of the ways bacteria, viruses and fungi are spread. Knowledge of the transmission systems [including environmental transport and survival] of many BAC is incomplete; thus we need to greatly enhance our data and models for the ability to effectively predict and anticipate the extent of an epidemic following a bioterrorist event, and control the outcome and exposures where possible. The new challenges for homeland security require improved levels of specificity regarding the infectious agent and assessment of exposure. Methodologies for BAC detection. in air, water, and on surfaceswill need sensitivity at the level and extent of exposure to be relevant to health outcomes.
CAMRA principal investigators all have experience with many of the category B and C BAC and have been involved in MRA for enteric bacteria (*E. coli* 0157H7) protozoa (*Cryptosporidium* and *Giardia*) and viruses (enteroviruses, Adenoviruses) via foodborne and waterborne exposures. Thus the models and risk framework have been investigated, produced and peer-reviewed and can be readily addressed by CAMRA in the case of a specific event or identified need. However, the MRA data, models and frameworks for the category A agents of concern are less well developed and will be the focus of CAMRA.

The outcomes and benefits to science will be evaluated using both traditional quantifiable measures, as well as in more qualitative and descriptive terms. All CAMRA projects will be expected to produce peer-reviewed publications. The development of new methods, models and tools will also be used as quantifiable measures of productivity. CAMRA is based on a model for interdisciplinary research, and integration of the results of each project will forge new scientific approaches to assessing microbial and infectious disease risk. One of the clear goals of the CAMRA is knowledge transfer: contributing to solving health problems, preventing exposure and illness, and addressing key questions of greatest uncertainty. CAMRA efforts will be at least partially focused on having an impact on the "state of practice" in the MRA field. Review criteria will also include the extent of interaction and collaboration with industry, federal and local government groups including EPA and DHS. We anticipate that CAMRA will produce at minimum the following: 1) Living document on the sensitivity and specificity of methods and their ability to address levels of safety. 2) In-use validation of methods. 3) Toolbox with validated surrogates for BAC. 3) Platform to assess the fate and transport of bio terrorist agents water distribution systems, air and buildings. 4)Validated models for characterizing exposure via aerosols and the indoor environment. 5) Inventory of critically analysed dose-response relationships for Category A agents. 6) Validation where outbreak data can be obtained. 7) Mechanistic dose-response models (based on physiological-based, dose-response). 8) Stochastic and deterministic dynamic disease transmission population models (accounting for heterogeneity in exposure) 9) Models for assessing controls (eg. vaccines, quarantines, decontamination, clinically intervention and treatment) 10) Goals for decontamination based on risk and safety. 11) A framework that incorporates risk assessment data, evidence and science-based information for decision makers eg. government officials, health providers and first responders. 12) Risk communication priorities to offset counterproductive public perceptions before and after a bioattack.

Management and Communication Plans

Management within CAMRA Dr. Rose (MSU) and Dr. Haas (Drexel) will serve as co-directors of CAMRA. Dr. Rose will direct from the lead institution and will be responsible for the financial management of the center and will serve as the quality assurance officer for the overall Center. She will be responsible for overseeing the integration team efforts (including the travel budget associated with project and integration team meetings) as well as specifically interacting with projects focusing on methods issues and educational programs. Dr. Haas will be responsible for overseeing and interacting with all projects and the associated quantitative data and models. Each co-director will have administrative support. Each project will be lead by a project leader who will be responsible for the communications between the project investigators and Executive Steering and Integration team (ESI).

Key to the success of CAMRA is the activities of the ESI team, who will meet at least twice per year. ESI Team

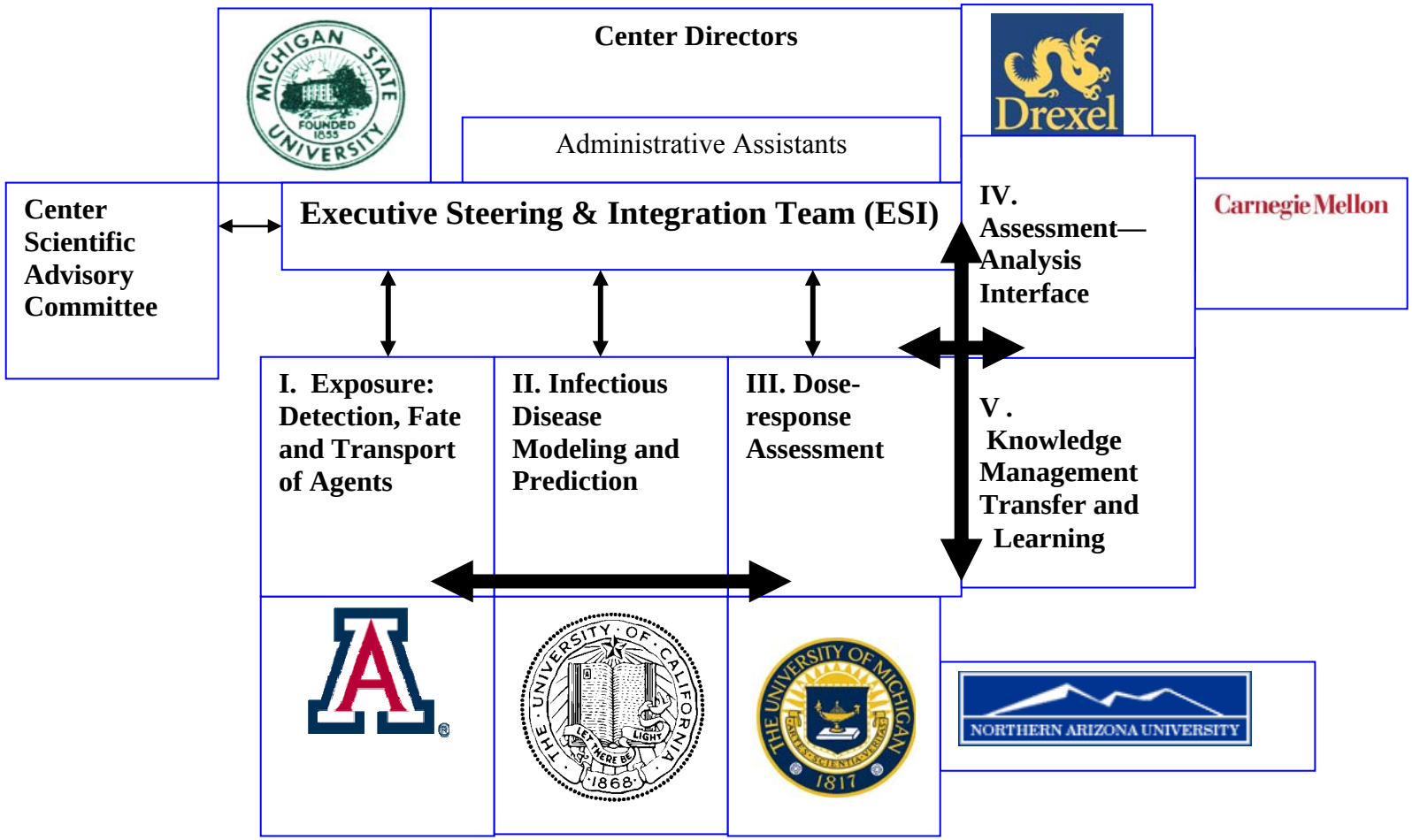
Institution	MSU	Drexel	UC	UA	U. MICH	CMU
Individual	Rose	Haas Weber	Nicas Eisenberg	Gerba	Koopman	Casman

This ESI team will have dual purposes. First they will represent the institution and assist in the integration of communication and educational components of CAMRA, but more importantly they will serve to examine the overall objectives of the center, the progress and the integration of the various project data and outcomes. Minutes, action items and outcomes will be recorded during the meetings. ESI team will also be responsible for producing published manuscripts and various reports via the integration of all projects. The cross linkages of the investigators and projects can be viewed via the type of agent (Table 1) and the structure of the CAMRA (Figure 3; 2004) as well as via the ILSI MRA framework (Figure 4, ILSI, 1996).

Table 1. List of some microorganisms important to CDC, EPA, HHS, and DHS and addressed by CAMRA Projects (EC-emerging concern)

Microorganism	CDC	Projects & BAC focus				
		I	II	III	IV	V
Bacillus anthracis	A	✓	✓	✓	✓	✓
Yersinia pestis	A	✓	✓	✓	✓	✓
Francisella tularensis	A	✓	✓	✓		✓
Coxiella burnetii	B			✓		✓
Variola major (smallpox)	A		✓	✓	✓	✓
Viral hemorrhagic fevers:		✓		✓		✓
Arenaviruses	A	✓		✓		✓
LCM, Argentine hemorrhagic fever (Junin -arena virus), Machupo virus, Guanarito virus, Hantaviruses, Dengue	A					
Ebola (filovirus)	A	✓		✓		✓
Marburg Virus	A			✓		✓
Rift Valley Fever virus	A			✓		✓
Hepatitis A	B	✓		✓		✓
Coronaviruses (SARS)	EC	✓	✓	✓		✓
Norwalk Virus	EC	✓	✓	✓		✓

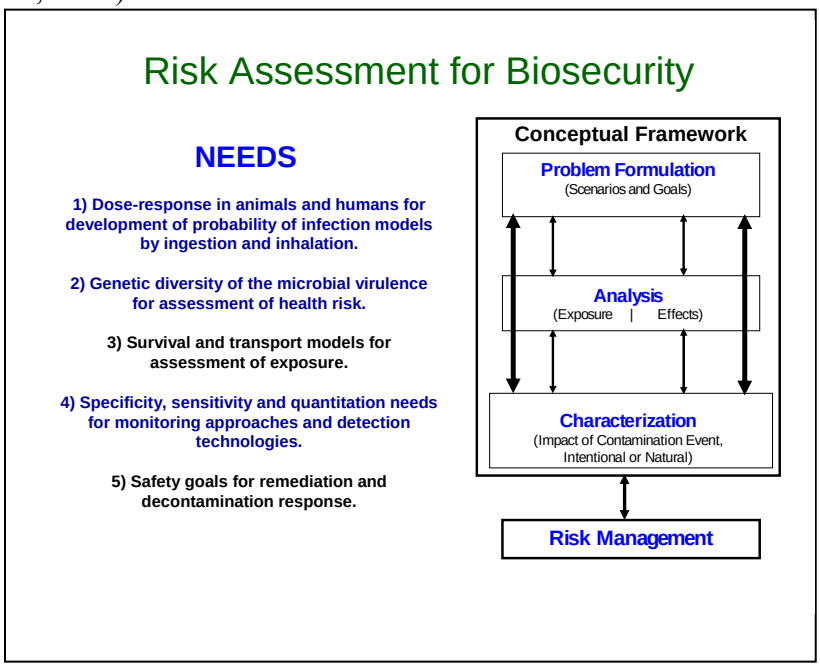
Figure 3. CAMRA Structure



Projects I, II and III will focus on aspects of the more traditional National Academy risk framework (NAS) and interact directly with each other. Projects IV and V will link across all three of these projects and will interact directly with the ESI team as well. Uncertainty analysis is a significant part of risk assessment, and Project IV team will be responsible for this effort.

Figure 4. ILSI Framework (ILSI, 1996)

Dr. Rose, Dr. Haas, Dr. Gerba and Dr. Eisenberg were all part of the original ILSI workshop that produced the MRA framework. Note that population modeling (the approach for integrating dose-response, exposure, individual and population models) as well as management options, are not features of this structure.



Project IV will also be responsible for examining various CAMRA products, communication of those products and identifying data and research needs. For example, Dr. Casman (CMU, project IV) has published on the evaluation of microbiological diagnostic tools for bioterroism agents (Casman, 2004), and can use a similar approach to assist integration of group I detection methods levels of sensitivity with group II dose-response models to evaluate the levels of "safety" that current and new environmental biosensors can afford. Dr. Koopman (U.Mich, project II) has published on population transmission of smallpox as well as impacts of vaccination (Koopman, 2003; 2004). Through interaction with groups I and II (dose-response and population heterogeneity), this model can be enhanced. Project IV (behavioral realism) will also assist in this analysis.

The proposed center will be organized such that knowledge management and transfer (project V) is integral to the design and conduct of the research, and the responsibility of all investigators. However, the expertise of Dr. Rosina Weber will guide this process utilizing the principals of computational intelligence and frameworks that will assist in meta analysis of data bases. **Dr. Weber will meet with each University team in the first year to assist in both the communication and learning process needed to build and utilize these programs.** Inherent in the problem-driven approach we have outlined, is the expectation that investigators focus their activities by understanding how to build fundamental knowledge that provides a foundation for addressing the MRA framework. This will be accomplished by use of a co-learning model,

whereby we initiate a dialog at the research design stage. Because the various disciplines that are involved in building the data bases for MRA, all use different languages, models and type of information, building a management and transfer system that will lend itself to communication with a variety of user groups is essential.

The core research program of the proposed center will be designed to develop fundamental understanding of environmental transfer of BAC and potential health outcomes. New knowledge will be the priority.

An important component of the knowledge transfer program will be to both encourage and assist investigators in communicating their results to the broadest possible professional audience, in addition to their peer research community. Selected findings that are likely to have widespread interest will be prepared as research briefs, review articles, web pages, and trade magazine articles, as appropriate. Other knowledge transfer approaches that we have experience with include conferences and seminars, videotapes, training manuals, software, patents, and specialty equipment. Where appropriate, resources will be devoted to these types of products.

Internal and external educational programs will be developed. This will be managed by Project V leader Dr. Ewen Todd, however, input from all the institutions will be important and will be achieved with direct communications and via the ESI team.

The Principal investigators of CAMRA and some highlights of their Expertise Many of the investigators in CAMRA have previously worked together and published together in various fields of microbiology, environmental ecology, risk assessment and disease transmission. This will enhance the integration and workings of the Center. Their expertise is complementary and will achieve collateral benefits.

Dr. Rose, co-director (MSU) has worked with Dr. Haas since 1988 and is a co-editor along with Dr. Haas of the only book on MRA, *Quantitative Microbial Risk Assessment,* (John Wiley and Sons, NY, NY, 1999). She has been involved with integrated microbial risk assessment models with Drs. Casman and Small and has worked with Dr. Gerba on MRA as well as on methods and transport assessment for bacteria, parasites and viruses. She has been involved with EPA and development of the methods and data for support of various rule making including the *Enhanced Surface Water Treatment Rule*. Her recent collaborations have examined zoonotic pathogens with Dr. Carole Bolin and Biochip development with Dr. Syed Hashsham.

Dr. Haas, co-director (Drexel) was one of the first scientists to examine dose-response data sets for microbial agents spread through environmental means and implement a quantitative risk framework following the NAS. He was the primary editor behind the book on *Quantitative Microbial Risk Assessment.* He has interacted with EPA in regard to disinfection and rules for development of the *Surface Water Treatment Rule*. He has examined outbreak data, inhalation, ingestion and contact exposures. He has recently published on dose-response modeling for anthrax. Dr. Haas has been a member of several National Research Council committees dealing with bioterrorism. He served on a panel to review the EPA research strategy for homeland security protection of water and wastewater infrastructure He is currently serving on a committee to define :"how clean is safe" following clean up from a bioterororist event.

Dr. Bolin is doctor of veterinary medicine. She has worked specifically with select agents and studied zoonotic disease transmission for over a decade. She has examined emerging zoonosis and patterns of infection and the external conditions involved with the spread of disease amongst different animal populations. She has collaborated with Dr. Rose on the subject of waterborne zoonoses.

Dr. Casman (CMU) is the Co-PI for current NSF project: "Integrating Risk Analysis and Risk Communication" section on Pneumonic/Bubonic Plague. She has developed an integrated risk model for cryptosporidiosis outbreaks and (with others) a bounding analysis technique for supplementing risk assessment. She is the PI on a CDC project: The Potential of Next-Generation Microbiological Diagnostics to Improve Bioterrorism Detection Speed; and a Co-I of a MacArthur Fdn grant to study bioattacks, detection, and response
She is involved in an NSF project on SENSORS: Placement and Operation of an Environmental Sensor Network to Facilitate Decision Making Regarding Drinking Water Quality and Security.

Dr. Choi (UA) has been working with Dr. Gerba for the last 4 years. He has been involved in the development of risk models for the contamination of produce by irrigation of water contaminated with pathogens. He has also studied the survival of pathogens in soil, water, on produce and biosolids.

Dr. Eisenberg (UCB) is an expert in the area of microbial risks and study of disease transmission models for water. He has collaborated with Drs. Rose Haas and Dr. Koopman in the past, in addition to being involved with the scientists from UCB. His current research interests include the epidemiology of waterborne pathogens and malaria. He has been involved in examining impacts and approaches for controls for environmentally transmitted agents and serves as an advisor to both the national and international communities of public health professionals.

Dr. Gerba (UA) is well known for his research on virus transport in water. He has been involved in survival and transport studies; point-of-use (POU) disinfection, prototype devices for UV disinfection. He has been involved in methods development and assessment for microbial detection in water and quantifying dispersion of biological agents in biosolid aerosols and domestic environments. He is PI of the Environmental Dispersion of Biological Agents in Sewer systems study for DARPA and the Alternatives for chlorine disinfection of water supplies study for the Dept. of Homeland Security SARPA He is also studying the dispersion of spores in drinking water distribution systems.

Dr. Gurian (Drexel) has developed integrated model of exposure, risk, and impacts of alternative regulatory options for multiple drinking water contaminants and is Co-PI of an NSF-sponsored study of risk management for extreme events affecting the U.S.-Mexico border-crossing infrastructure. He is currently involved in two studies of the public perception of technological risks, one addressing the perceived risk of wastewater reuse and one addressing the perceived risk of carbon monoxide poisoning, and a third study concerning Bayesian hierarchical modeling of the occurrence of contaminants in drinking water.

Dr. Hashsham (MSU) is a civil and environmental engineer who specializes in the development of bio-molecular tools for the assessment of environmental contamination. He has been awarded an NIH grant to address validation experimentation of a biochip for Class A agents and is the Co-investigator on a project for the development of a biochip for water funded by EPA. He has been collaborating with the Center for Food Safety and Toxicology on the characterization of enteric bacteria and has established research program with Dr. Rose in water. He is an expert on the design and validation of molecular tools including microarray technology.

Dr. Keim (NAU) is a geneticist and a forensic ecologist. He has used molecular methods in investigating plague population genetic structure, characteristics of *Francisella tularensis*, and the molecular epidemiology of anthrax, particularly the 1993 incident in Kameido, Tokyo. He has begun some collaborative efforts with Dr. Gerba.

Dr. Koopman (UM) is an infectious disease expert who has worked in the medical arena on pediatric disease such as the spread of rotavirus in developing and developed countries. In the last decade he has built a program on using mathematical and statistical approaches to the study and description of epidemiology. He has worked directly with EPA on population modeling and has address a number of select A agents. He has collaborated previously with Dr. Eisenberg, Dr. Haas and Dr. Rose.

Dr. Nicas (UCB) is an industrial hygienist working with aerosols in particular. He develops mathematical models of contaminant emission and dispersion in air and probability models of airborne infectious disease transmission. Based on risk analysis, he has evaluated respiratory protection against airborne pathogens used for bioterrorism. He has collaborated with Dr. Eisenberg and other scientists at the University of California, Berkeley.

Dr. Small (CMU) is a member of EPA SAB, Environmental Modeling Committee; FIFRA SAP; EPA BOSC (1996-2002). He is an elected Fellow of Society for Risk Analysis (SRA); Associated Editor of *Environmental Science & Technology*; Co-Editor of:McDaniels and Small. 2004. *Risk Analysis and Society: An Interdisciplinary Characterization of the Field*. Cambridge University Press, Cambridge, UK. Co-PI for current NSF project: SENSORS: Placement and Operation of an Environmental Sensor Network to Facilitate Decision Making Regarding Drinking Water Quality and Security. Co-author of: Ramaswami, Milford, and Small. *Integrated Environmental Modeling: Pollutant Transport, Fate, and Risk in the Environment*, Wiley, in press.

Dr. Todd (MSU) is the Director of the National Food Safety and Toxicology Center, where he coordinates research in microbiology, toxicology, epidemiology, risk assessment and social science in the area of food safety, distance education programs, and outreach in the community. Dr. Rose, Gerba and Haas first met Dr. Todd while he worked in the Health Products and Food Branch, Health Canada, Ottawa where he was active in assessment of foodborne disease and instituted an MRA program. He is currently Chair of the Food and Water Specialty group in the Society for Risk Analysis.

Dr. Weber (Drexel) specializes in studying the design and implementation of computational intelligence methods (e.g., Case-Based Reasoning, Fuzzy Set Theory, Information Extraction,

Machine Learning) to solve knowledge management problems in a wide variety of domains (e.g., Law, Military, Nutrition, Medical, Finance). From 99-01, she worked with the Navy Center for Applied Research in Artificial Intelligence (NCARAI) in the Naval Research Laboratory (in Washington, DC) funded by ONR grants, where she developed knowledge-based methods for improving the efficacy of repository-based knowledge management systems, such as the Navy Lessons-learned System. Since 2001, she is an Assistant Professor in the College of Information Sciences and Technology at Drexel University, where she teaches courses related to Computational Intelligence and Knowledge Management.

CAMRA Scientific Advisory Committee. This committee will be science-based. It will be made up of four to five outside experts in fields such as epidemiology, biosensors, modeling, environmental microbiology, communication, biosecurity and may be involve individuals from government or academia but who will be chosen for their scientific expertise. An international member will be considered. This will be a mix of professionals in 1) public health (eg. Dr. Art Reingold, Dr. Tomas Aragon, Dr. Jack Colford, all from UCB; CDC Dr. Deborah Levy; Dr. Paul Hunter, from PHLS in England). 2) Environmental microbiologists, (Dr. Suresh Pillai; Dr. Mark Sobsey) 3) Risk assessment/analysis, eg. Dr. Paul Gale; 4) Disease transmission, (Dr. Travis Porco here at the CDHS, experts in Class A BAC, eg. smallpox) and/or 5) clinical microbiologists.

The role of the advisory committee will be providing advice on 1) the Project programs and specific objectives; 2) advice on integration and 3) and advice on communication. They will meet with the ESI team once per year.

Communication and Activities Outside the Center

One of the goals of CAMRA is to build collaborations and communications with researchers, educators, government and community officials who may be interested in or users of the MRA data, information, tools and frameworks. We will establish linkages with the other centers for DHLS (Table E-2) where appropriate. We currently have links as a partner institution to the Center for Food Protection and Defense, and MSU is playing a major role in the education program framework in which CAMRA can become a partner. We have also received a letter of interest from Center for Foreign Animal and Zoonotic Disease Defense.

As individuals, the investigators of CAMRA have built collaborations throughout the US and world, collectively we will build stronger relationships with organizations (International Food Institute) government groups (US Army Center for Health Promotion and Preventive Medicine) and international research institutions (University of Cordoba, Spain, Canadian Early CBRN Attack Detection by Computerized Medical Record Surveillance) [see letters of support, Appendix A]. Thus knowledge repositories can be shared with the larger scientific community interested in MRA.

Table 2 Department of Homeland Security Centers of Excellence.

Center	**Purpose**	**Lead Institution**	**Partners**
Homeland Security Center for Risk and Economic Analysis of Terrorism Events 3 yrs 2003	Study of risk analysis related to the economic consequences of terrorist threats and events	University of Southern California	University of Wisconsin at Madison, New York University, North Carolina State University, Carnegie Mellon University, Cornell University, and others
Homeland Security National Center for Foreign Animal and Zoonotic Disease Defense 3 years 2004	Address potential threats to animal agriculture including foot and mouth disease, Rift Valley fever, Avian influenza and Brucellosis	Texas A&M University	University of Texas Medical Branch, University of California at Davis, University of Southern California and University of Maryland, Homeland Security's Plum Island Animal Disease Center
Homeland Security Center for Food Protection and Defense 3 years 2004	Study agro-security issues related to post-harvest food protection	University of Minnesota	Michigan State University, University of Wisconsin at Madison, North Dakota State University, Georgia Institute of Technology, Rutgers University, Harvard University, University of Tennessee, Cornell University, Purdue University and North Carolina State University and major food companies

Through the educational program (Project V) workshops and/or on-line courses could be developed for key user groups including CDC laboratory response network once data, frameworks and products are forthcoming to integrate MRA principals and tools into the integrated network of state & local public health, federal, military, & international labs that are established to respond to bioterrorism.

Addressing the Future Issues

One has only to read the headlines to realize that there are growing concerns regarding the spread of infectious diseases and our ability to control them. Our sensitive populations (elderly and immunocompromised) are increasing in numbers in many of our communities. The flu vaccine shortage has provoked a reexamination of public health priorities and practices. The assumptions and methodologies of the last century need to be revised in light of demographic and security projections. CAMRA microbial risk assessments will be structured to incorporate new developments.

In addition to risks from pure cultures of living microorganisms, CAMRA collaborators have a strong interest in risk frameworks for BAC such as *Clostridium botulinum* toxin. In addition, the

potential risks associated with the exposure to a mixture of BAC will be examined using quantitative risk methods. There are new BAC which have been inadequately studied. Recent reports have suggested that the organism *Burkholderia pseudomallei* (the causative agent of melioidosis) is a significant potential choice for bioterrorism (it survives in the environment, could be spread by aerosols, can be acquired from the natural environment and causes mortality) yet very little quantitative data are available to address this BAC from a MRA perspective.

CAMRA will begin an incident watch and develop an incident fund for addressing emerging and important BAC. Thus as the programs evolve at CAMRA, if emerging national events occur or new specific data and information can be gleaned from some natural or intentional disease outbreak, a team of microbial risk assessors can be mobilized to develop a research agenda to advance our understanding of the disease processes and controls that will be needed to face new threats in the future.

Program Evaluation

CAMRA will utilize a logic model over time to address establishment of program direction, implementation, an evaluation framework and outcomes. MSU programs have experience with the logic model system and have utilized the guide produced by the W.K. Kellogg Foundation (W.K. Kellogg Foundation Logic Model Development Guide, www.wkkf.org) for this purpose. Thus this will help to address the resources, operations and future activities, as well as provide a framework for examining how well we are doing.

The program will be evaluated by 1] resource and inputs, 2] activities, 3] outputs 4] outcomes and 5] impact. While assistance can be obtained via a professional evaluator, the ESI team and advisory committee as well as stakeholders from the various user communities of the MRA data, information and knowledge repositories will be valuable in developing a collaborative process for both evaluating and maintaining a successful program.

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Project I. Exposure: Detection, Fate and Transport of Agents

Introduction

The overall goal of this project is to improve our ability to quantify exposure to biological agents of concern (BAC) in indoor environments and via the water supply. The greatest amount of uncertainty in quantitative microbial risk assessment is quantification of exposure (Haas et al 1999). The number of organisms to which an individual may be exposed may vary by orders of magnitude depending on the particular environment and properties of the organism. This information becomes even more important for organisms that may be released into environments where they do not occur at all or in significant numbers as to pose a risk. The goal of this effort is to determine the fate and transport of BAC in selected environments where the exposure impact may be large or complex. Two major areas are:

- Indoor building environments
- Drinking water distribution systems

Because BAC agents are too hazardous to work with, in the environments we wish to study, it will be necessary to develop surrogates so that assessments can be made under real world conditions. This project draws together several groups with extensive experience in the detection, transport and fate of BAC in aerosols, water and fomites, and transmission dynamics of Category A agents. This goal will be met through a series of specific sub-project objectives.

1. Development of new BAC surrogates for application in methods assessment and transport and fate modeling efforts.
2. Validation of detection methods for microbial risk assessment.
3. Development of fate and transport models for BAC on fomites.
4. Development of fate and transport models for BAC in water systems.
5. Development and validation of a discrete-time Markov chain model for airborne BAC within a room.
6. Measure the re-suspension of particle-associated BAC in a test room or chamber
7. Determine the particle size distribution of respiratory aerosol

Objective 1. Development of new BAC surrogates for application in methods assessment and transport and fate modeling efforts.

To understand the fate and transport of BAC in the real world it will be necessary to develop and select surrogate organisms whose properties would impart behavior in the environment similar to that of the BAC. These would include i) Surface properties (isoelectric point and hydrophobicity), ii) Environmental resistant structures (spores, cysts), iii) Size and shape, iv) Similar nucleic acid, and v) Resistance to desiccation and disinfectants. Surrogate development will also be used for the assessment of the sensitivity of methods for the detection of BAC in real world environments.

There are several types of surrogate models, which can be used. These include

- Polystyrene spheres of various sizes
- Viral like particles (VLP's) identical or similar to the virus of interest. Nucleic acid of non-pathogens can be inserted into these particles for assessment of detection methods

- Live vaccines
- Genetically related organisms
- Model organism (bacteriophages of similar structure and nucleic acid as BAC)
- Indigenous organism
- BAC or related organisms inactivated by disinfectants that do not effect transport properties (i.e. UV light inactivated spores)

The University of Arizona group has previously used polystyrene spheres to trace the transport of bacterial and viruses indoor and aquatic environments (Bales et al 1997; Gerba, unpublished). Viral like particles have been developed for almost all of the BAC including Ebola virus, arena viruses, hantavirus virus (Table I-1). They have been used in several studies to assess the environmental transport of pathogenic viruses (Cabellero et al 2004). Bovine rotavirus VLP's have been demonstrated to have the same stability as the infectious virus produced in cell culture (Loisy et al 2004) in aquatic environments. Live vaccines are available for almost all of the bacterial agents of concern, and where they cannot be used, closely related organisms could be used (i.e. *Bacillus cereus* or *B. thuringiensis* spores for anthrax spores). Bacteriophages have been used in numerous studies to assess the survival and transport of viruses in water and indoor (households and day care centers) environments (Rheinbaben et al 2000). The movement of naturally occurring infections via fomites can also be assessed by routine monitoring of building fomites as the infections spread through a community. We have been able to determine the distribution of influenza virus in homes and day care settings by monitoring influenza viruses on fomites by PCR (Boone and Gerba 2004). This approach helps identify those surfaces that become contaminated during the natural spread of either a respiratory or enteric organism. Table I-1 provides existing examples of each type of surrogate.

An initial goal of the exposure group will be to evaluate potential surrogates for use as models for the various BAC agents in different environments. This will be done by the University of Arizona (UA) and Northern Arizona University (NAU) groups through an assessment of safety, literature reviews, and similar behavior to BAC in the same environment, and similar properties that would control survival and distribution in the environment. Selected surrogates will initially be assessed in laboratory experiments before field or large-scale use. The group at NAU will conduct laboratory experiments to compare (benchmark) the survival of *B. antrhracis* and *B. thuringiensis* to determine the latter's potential usefulness as a surrogate. The experience of the NAU group working with *Yersina pestis* and *Francisella tularensis* and other BAC will also be relied upon in the selection of surrogates (Johansson et al 2004; Girard et al 2004). The UA group will develop VLP for arena virus (Category A) and Norwalk (Calicivirus) virus Category B)(Redman et al 1997). This part of the project will provide surrogates which could be available for others investigators outside of the center activities.

Table I-1. Examples of surrogates for BAC

Potential Surrogates	Pathogen	References
Polystyrene Spheres	Viruses, bacteria, parasites	Bales et al 1997
Virus-like Particles (VLPS)	Ebola virus, Hantaan virus, Semliki-forest virus	Watanabe, et al 2004 Betenbaugh, et al 1995 Notka, et al 1999 Mossienko, et al 2003
Live Vaccines	*Yersinia pestis* *Francisella tularensis* *Coxiella burnetii*	Titball and Williamson, 2004 Conlan, 2004
Genetically Related Organisms	*Bacillus subtilus, B. thuringiensis* *B. anthracis*	Nicholson and Galeano, 2003 Hill et al 2004
Model Organisms	Coliphage MS-2, non-lipid viruses	Utrup and Frey, 2003
Indigenous Pathogens	Influenza, viruses	Boone and Gerba, 2004

Objective 2: Validation of detection methods for microbial risk assessment

Development of tools to quantify risk requires that we have detection methods that are able to: i) detect single cell/particle for bacteria/viruses, ii) process large number of samples (compounded or separate) to provide data on spatial variability and address sampling limitations for the chosen method, iii) perform the tests in less than 1 hour under field conditions, although it may be longer during the developmental stage of the risk methods, and iv) quantitatively incorporate the false positives and false negatives error rates. Table I-2 lists the desired range of values for these characteristics and examples of studies/devices that are currently available to achieve those. It is obvious that all of the above must be with surrogates that closely mimic the real threats with respect to parameters listed in Table I-2 but are not harmful if used for modeling release scenarios and testing detection methods (e.g., see Schaefer et al., 1999). Availability of these surrogates with fluorescent tags (e.g., see for viruses, Gitis et al, 2002) to improve their detection limit will also be required.

Establishment of the already available high throughput, fast, sensitive, and specific detection methods will be one of the objectives of the project focusing on exposure, fate, and transport of the target surrogate agents. The focus of validation will be on surrogates for the Category A agents (Table E1 see Center management) so that risk from contaminated air, water, soil, and hard surfaces from indoor and/or outdoor environments can be quantified. From many methods reported in literature for the Category A agents, it is evident that most of the targets have a number of detection methods that can provide results within hours (some within a few minutes, Reference from Science). Some of the methods are also quantitative (e.g., real time PCR using genes specific to *Bacillus anthracis*) and claim to detect at the level of one cell or one spore (Ref). When using RT-PCR, it is also possible to identify methods that multiplex either dozens of genes of the same target or dozens of targets (Ref). Therefore, development of new detection methods for the above agents will be outside the scope of this effort. Improvements in the existing detection methods with respect to all the five parameters listed in Table I-2 for the specific purpose of improving the quantifying the risk will, however, be included in the scope.

Table I-2. Desirable characteristics of detection methods for quantitative microbial risk assessment

	Parameter of interest	Desirable value	Comments
1.	Detection limit	1 -10 cells/particles	Schaefer et al., 1999, -Nam et al., 2003, 2004
2.	Test speed, minutes	5-60	Belgrader, P., et al. 1999, PamGene
3.	Sample throughput	100-400,000	ABI 9700, 454 Corporation
4.	False positives and false negatives	1 in 10,000,000	If possible, this should even be higher
5	Cost per sample	$1-10	Many single agent tests, PCR

Major gaps are in the area of how these methods are used in the field to quantify risk based on the occurrence and abundance of a target organism or gene. The whole system from sampling, sample processing, and detection must work together to yield useful data for quantification of risk. Such systems are neither fully developed nor well tested. We will establish the baseline in terms of the number and type of samples, detection methods including limits of detection, the false positive and false negative error rates, and the actual detection technologies. Processing of large number of samples of different types in a multiplexed manner, quantification of abundance of a large number of target genes in each sample, and the associated magnitude of false positive and false negative error rates under field conditions will also be developed.
We will also develop protocols to identify the most likely hot spots for the presence of an agent as indicated by the mode of contamination, and likely will generate hypothetical data to develop methods for risk quantification. We will use the best available sampling and detection tools to experimentally validate the quantified risk for each type of environmental release scenario in model systems (fomites, building, and selected animal models).

The major questions related to method validation will include the following:

i) What are the best available methods for each of the six Category A agents with respect to specificity, sensitivity, speed, genetic variability, cost, sample processing, false positives, false negatives, ease of use, ability for on-the-spot analysis, etc. Can they be carried out together on-the-spot or off-line for fast screening?

ii) Are there existing methods using surrogate and/or DNA tagged nano-particles that can be used to begin the release and modeling exercises in year 1 of the center activities. Our initial survey indicates that they do exist (Nam et al., 2003, Nam et al., 2004, Amagliani et al. 2004, Dunbar et al. 2003, Francois et al. 2003, Gitis et al., 2002) but further improvements/changes may be necessary for our specific purpose.

iii) What is the minimum number of samples (including locations) that is needed by the risk assessment tools to provide the necessary confidence in "clean up operations". What equivalent sampling locations and number of samples would have missed the detection and resulted in exposure?

iv) What is the potential of high throughput sample processing approaches/units in minimizing the uncertainty associated with a limited number of samples?

v) What is the impact of gene sequence based detection in evaluating risk? What methods are best suited for detection of viability?

Objective 3. Development of fate and transport models for BAC on fomites

Fomite contamination is believed to play a role in 80% of the common infections that we experience (respiratory and gastrointestinal). Ingestion of soil (pica) or mouth contact with inanimate objects (fomites) or indirectly by contamination of the fingers, (which are then bought to the mouth, nose or eyes) are additional routes of transmission. The effectiveness of transmission by fomites is complex (Haas et al 1999). Resuspension of organisms from fomites will be dealt with by the University of California (UC)group in objective 6.To model this, an understanding of the number of organisms transferred during each step is necessary, as well as, the survival of the organisms on the surfaces. Survival and transport depend upon a number of factors including i) Humidity, ii) Suspending media, iii) Type of organism, iv) Temperature, v) Type of surface, and vi) Moisture on the surface.

The area most lacking information is on the degree of transfer from hands to mouth, nose, eyes, other fomites, and foods. The UA group has previously conducted limited study on the transfer efficiency of surrogate bacteriophage and bacteria from fomites-to-hand-to-lips of human subjects for the use in risk models (Rusin et al 2002). To better develop quantitative data we propose to

- Use surrogates to assess transfer rates for hands for items which may be involved in bioterrorist acts i.e. envelopes, produce, office items, etc (UA group)
- Study the transfer of viral like particles and spores that resemble the surface properties of BAC from surfaces-to-hand-to-lips or food items (UA group)
- Study the dispersion of surrogates in different types of working environments i.e. offices, warehouse, package handling facility. Surrogates similar to those previously used in child day care centers will be used (Rheinbaben et al 2000). UA and UC groups.

The qualitative information developed in these studies can used in risk models to assess exposure of BAC in different indoor environments.

Objective 4: Development of fate and transport models for BAC in water systems.

The primary goal of this work is to experimentally determine quantitative exposure if a BAC is released into a drinking water in a water distribution system. The release of BAC into drinking water or irrigation water used for crop production ~~or~~ can have a far-reaching impact on the environment (Morris et al 1998; Luthy 2002; Deininger et al 2000; Decker 1990),. For example, release of BAC into the drinking water distribution system will not only effect the drinking water, but potential indoor air, food, and surface (fomite) contamination (Figure I-1). Contaminated buildings, sewer systems, sewage discharge areas, and biosolids produced from sewage would all pose infection disease risks (Hoglund et al 1998; Mail and Asmad 2002).

The University of Arizona is currently constructing a drinking water distribution system to a group of four existing dwellings, which will serve to assess the detection and fate of BAC and chemical agents in distribution systems. It is being constructed with funding from Tucson Water (the utility which serves Tucson) the National Science Foundation Water Quality Center, and The University of Arizona to serve as a model community for the testing and evaluation of real time monitoring of intentional chemical and biological intrusions. The “Water Village” as it will be called will provide the ability to assess the dispersion of BAC in the distribution system and within buildings. It will also aid in determining the assessment of clean-up methods (i.e.

disinfectants). The distribution system will contain sensors for water quality (pH, temperature, dissolved solids, etc) throughout the network for continuous monitoring. It will also be possible to change the water at various points in the distribution system and remove sections of piping for testing and observation. Water use in the homes (kitchen tap, showers) will mimic that in an actual family. It will also be possible to do aerosol release in these homes to assess dispersion and potential success of clean-up efforts.

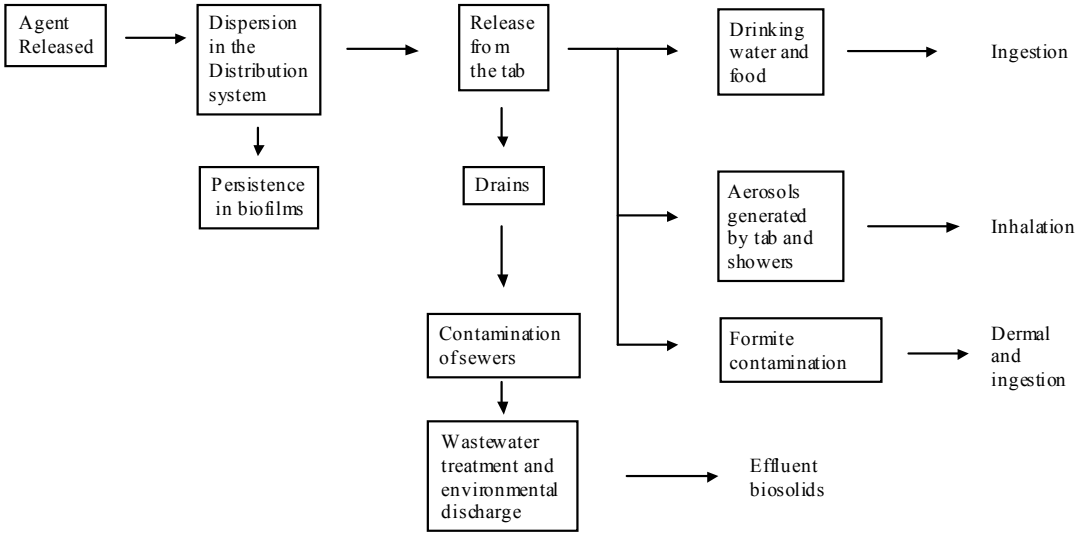

Figure I-1. Potential environmental impacts from release of a BAC in drinking water distribution systems

It is proposed that surrogate viruses and bacteria be released into the distribution system to assess dispersion, persistence, and distribution of surrogates. This would be followed over time and decontamination success and impact on risk reduction can be evaluated. Artificial Neural Network models will be used to assess the data for incorporation of risk assessment models.

Application of Artificial Neural Networks. A model based on an Artificial Neural Network (ANN) will be developed and tested (i) to forecast microbial dispersion patterns in each system, (ii) to estimate dispersion time, and (iii) to recommend detection methods, sampling frequencies, and sampling locations**.**

Prediction modeling through computational tools for irrigation water channels, drink water systems and sewer are currently underway at the University of Arizona. Based on a series of field experiments, the qualified computational model can provide us an impetus to establish an optimization technique in a systematic manner. The spread patterns of biological agents can be predicted by computational methods upon experimental verification. Numerical data sets can serve as a database for microbial risk assessment.

We propose to use the ANN as a flexible mathematical structure that is capable of learning complex systems with approximating multiple input and output responses. Simulations of the transport and dispersion of chemical tracers and microbial contaminants have been successfully carried out using ANNs in recent years. Our goal is to produce a ‘well-trained’ neural network to predict the release point and release time of contaminants by tracing back their detection data at monitoring points.

We will evaluate the limitations and uncertainties characteristic of special and temporal sampling and detection methods used to measure microbial occurrence in the environment.

We also would like to develop models that can be used to rapidly assess the risk based on detected biological agents introduced at different points in various environments (buildings, agricultural lands, food chains, and water distribution systems). The goal of this task is to provide decision-makers a simple tool to assess the impact of BAC.

Experimental approach. The major goal of ANN in this study is to predict the spatial and temporal identification of microorganism release in pressurized water systems and prediction of environmental dispersion using a concept of a pattern classification. To accomplish these, water quality parameters such as pH, temperature, alkalinity, turbidity, chlorine concentration, conductivity, and dissolved oxygen considered as key parameters. The ANN-based model will be used as the base of knowledge on the viability and infectivity potential of pathogens in water, identify and prioritize the key gaps, formulate a comprehensive approach for filling those gaps.

Artificial neural networks use a modeling philosophy that is similar to that of statistically based approaches, using historical data sets to approximate the relationship between inputs and corresponding output variables. A neural network consists of a system of interconnected nodes. The first layer of nodes (the input layer) brings the information to be processed into the network. Nodes in subsequent layers are called neurons, as they perform neuron-like functions. Each neuron consists of two parts, a linear summation function (Σ) and a linear or nonlinear activation function (f).

While many different types of neural networks have been developed, a back-propagation design will be chosen for the proposed research because of its demonstrated effectiveness at classifying nonlinear data sets. The simulated observations with computational simulation tools validated by experimental data will be used to train the ANNs. The standard back-propagation network has three types: input, hidden and output neurons. Input neurons send the initial data to layers of processing (hidden) neurons. Output neurons accept input from the hidden layer and provide the network's report to the user as a list of probabilities.

A set of input-output responses representing a variety of simulation scenarios is sampled at random, and a simple technique to allocate this set into training and testing subsets is developed. Training procedures consist of two phases, a training (accuracy or calibration) phase and a testing (generalization or validation) phase. In the ANN's training phase, the objective is to determine the weights that minimize a specific error criterion defined to measure an average difference between the desired responses and the ANN's responses to the patterns. The success of the training strongly depends on the normalization of the data and on the choice of the training parameters, namely the learning and momentum coefficients (Demuth and Beale 1998; Water Science Technology Library 2000).

The networks' generalization properties can be exploited for the identification of parameters values associated to new simulated concentration histories. After training has been completed, the ANN's generalization properties will be used for various applications. For instance, the ANN can be used to identify the location where unknown biological agents are released with simulated concentration histories (Park et al 2003; Schleiter et al 1999; Yabunaka et al 1997; Maier et al 1998)..

Shortly after a purposeful contamination event, the off-line monitoring equipment will detect significant changes from the baseline in time-series of concentration of *E. coli*,

conductivity, pH, and/or turbidity – or more likely, one or more of these parameters. The ANN will interpret early-detected time-series data and predict the following pattern of water quality parameters. At the same time, the ANN will calculate characteristics and statistical variables, which can present a certain pattern which will be used to identify the contaminant source.

Possible Outcomes. Physical, hydraulic and biological characteristics in hypothetical conditions will be used for the ANNs' training. In all cases, the ANNs' approach will demonstrate the ability to identify the unknown parameters in the models that leads to concentration histories that are very similar to the computed values by the water quality model. On this basis, the ANNs will be able to trace back the concentration of hypothesized biological agents and will provide an approximate range for the releasing site, which is the pollutant source. The ANNs' results will be identified through recalculation by the water quality model. Statistical analysis tools will evaluate their performance.

A measure of the interdependence between the measured data and the model will be assessed through statistical analysis; for example, the sum square error (SSE), correlation coefficient (R2), root mean square error (RMSE) and mean error (ME). In addition, several additional variables will be presented for clear comparison: breakthrough time (travel time), peak concentration and peak detection time.

Knowledge of source areas can lead to the installation of typical security apparatuses (e.g., fences) and/or atypical security measures (e.g., armed security guards) that are most likely to be applied at large water supply systems. Unfortunately, it appears that much of the country is of the misconception that only very large water-supply systems are threatened and, furthermore, only at the downstream outflow points beyond the water treatment system. While this situation certainly is worthy of concern, it is not the only case that should merit our attention.

By conducting basic model simulation studies, water managers can also develop standard risk assessments for biological attacks on their drinking water supplies. By developing basic risk assessments, site managers can gain a general sense of how vulnerable their respective water supplies are to various toxic contaminants and release amounts. A vulnerability assessment can then be used to develop human health protection-strategies (e.g., "boil water" or "do not drink" health advisories) for use in the event of a terrorist attack.

We expect the proposed study can be critical to advance the assessment of fate and transport, outline numerical tools to represent their patterns, and improve the current surveillance system by integrating experimental and numerical approaches.

Objective 5: Development and validation of a discrete-time Markov Chain Model for airborne particle fate-and-transport within a room

This component has three aims. (1) Develop and experimentally validate a simple discrete-time Markov chain model (termed Level I) for the fate-and-transport of particles released into air. (2) Demonstrate a method for translating the velocity vector and turbulent diffusivity field outputs of computational fluid dynamics modeling into transition probabilities for a more complex Markov chain model (termed Level II). (3) Test the performance of the Level I Markov chain model against the performance of the Level II model in simulating exposure intensity to airborne particle-associated BAC. Combined with information on the infectious dose-response model (Haas, et al., 1999) and on the pathogen emission rate (for example, Nicas, Nazaroff and Hubbard, 2004) the resulting exposure model would permit estimating infection risk and intervention efficacy for different BAC in a variety of scenarios

(Nicas and Hubbard, 2002). For example, one could assess a health care worker's risk of secondary infection by *Y. pestis* bacilli (pneumonic plague) or variola virus (smallpox) emitted in respiratory aerosol from infectious patients; for these two BAC, infection can occur due to deposition of pathogens in either the upper respiratory tract or the pulmonary region (Meyer, 1961; Nicas, Hubbard, et al., 2004). Overall, the validated model would offer a relatively simple and intuitive approach to estimating spatially specific concentrations of airborne particle-associated BAC in indoor environments, and predicting the locations and amounts (e.g., hot spots) of surface contamination with BAC following a release of BAC into room air. This phase of the project will be conducted at the University of Calidornia.

Previous Work: Current models predicting exposure to airborne contaminants focus on gas-phase substances or small particles with negligible settling velocities. We have developed a simple (Level I) Markov chain model that describes the fate-and-transport within a room of mixtures of particles with different aerodynamic diameters released into air, as would pertain in many particle exposure scenarios (Nicas and Nazaroff, 2004). Particles are dispersed by turbulent eddy diffusion (assumed constant throughout the room) and by advective airflow (assumed uniform in one direction), and are removed from room air by gravitational settling, by exhaust ventilation (mechanical and exfiltration), and to a small degree by deposition onto walls. Each mechanism is assigned a first-order rate constant, where the constants for gravitational settling and wall deposition depend on the particle aerodynamic diameter. Room air is divided into cubic cells. An interior room air cell is bordered by six neighboring cells, two each along the x-, y-, and z-axis, respectively. For a time step Δt on the order of 10^{-3} min, a particle in a room air cell is assigned a probability of remaining in that same cell or moving to one of the six neighboring cells, where the probabilities depend on the first-order rate constants. The set of probabilities are entered in a square matrix **P**; each room air cell is represented by a row and column in the matrix. Settling, deposition and exhaust removal are also represented in the **P** matrix. The probability that a particle starting in cell *i* at reference time zero is in cell *j* at future time $n \times \Delta t$ is found by multiplying **P** by itself n times, or $\mathbf{P^n}$; the desired probability is the entry in the i^{th} row and j^{th} column of $\mathbf{P^n}$.

The model predicts the change in the size distribution and mass concentration of the aerosol as particles disperse away from the release point. The model also predicts the pattern of settling and surface deposition of different sized particles within a room. One of us has published details of a similar Markov chain model for gas-phase contaminants (Nicas, 2001) The difference here is that particles have additional first-order loss rates involving gravitational settling and deposition onto surfaces, and consideration is given to a mixture of different particle sizes.

Aim 1 – Our goal is to modify the Level I model to account for a thermal plume around the body and for objects within the room, and to test model predictions by direct experimentation.

Experimental Approach. At UC-Berkeley, initial experiments would be conducted using a chamber fabricated for this study, with dimensions chosen to permit examining particle behavior in a small-scaled room and to accommodate aerosol generation and sampling devices. Several ventilation configurations would be used. An aerosol generator would be located in the chamber, although particles could also be released into the supply air stream. We would initially use liquid ammonium fluorescein particles via a procedure previously described (Thatcher, et al., 1996), although later experiments would use solid polystyrene spheres or surrogate BAC particles developed at the University of Arizona, Northern Arizona University and Michigan

State University. We would generate monodisperse aerosols of different aerodynamic diameters. For each particle size, there would be different combinations of factors involving the number of chamber air changes per hour, the chamber ventilation configuration, and the presence or absence of a heating lamp to mimic the body's upward thermal plume. An experimental run would consist of the continuous emission of particles for a pre-determined length of time, T_1. Air sampling at the different chamber locations would be performed up to T_1 and would cease once particle release ceases. The chamber air exhaust supply would continue operating up to subsequent time T_2 at which point the experimental run would be terminated. The air filter samples and the chamber surface filter samples would be collected and analyzed for fluorescein. For the same set of room conditions and particle sizes, the Markov chain model would be used to predict the particle mass collected on the samples, such that the accuracy of model predictions could be evaluated over a range of particles sizes and room ventilation conditions.

Aim 2 – Traditional computational fluid dynamics (CFD) modeling of indoor air flow produces a velocity vector field and a turbulent diffusivity field as outputs. CFD is considered the most accurate modeling method to predict air gas-phase contaminant concentrations at different room positions. Our aim is to translate CFD output into a series of transition probabilities for a discrete-time Markov chain model, and thereby create a Level II model to predict the fate-and-transport of particle-associated BAC within a room. The general approach is described below given the simplifying context of a Cartesian coordinate system and a CFD grid consisting of cubic cells with neighboring cells adjoining surface-to-surface, that is, the surfaces of two neighboring cells abut each other completely.

Experimental Approach For a given node (cell), assume the velocity vector **v** is located at the cell origin with magnitude $|\mathbf{v}|$ (m min^{-1}) and direction angles θ_X, θ_Y and θ_Z along the x-axis, the y-axis and z-axis, respectively. The velocity component along the x-axis is $(|\mathbf{v}| \times \cos\theta_X)\mathbf{i}$, where **i** is the unit vector along the x-axis in the positive direction. The velocity components along the y-axis and z-axis are computed in an analogous fashion. The air speed (m min^{-1}) in each orthogonal direction is the value of the coefficient which multiplies the unit vector. Consider that a cubic cell with velocity vector **v** has length aspect L (m), such that a cell face has surface area L^2 (m^2) and the cell has volume L^3 (m^3). Consider that $(|\mathbf{v}| \times \cos\theta_X)\mathbf{i}$ is directed to the neighboring cell to the right. The air flowrate (m^3 min^{-1}) from the cell to the neighboring cell on the right is $|\mathbf{v}| \times \cos\theta_X \times L^2$. The corresponding first-order rate constant for a particle leaving the cell to the neighboring cell on the right due to this advective air flow is: $\lambda_X = (|\mathbf{v}| \times \cos\theta_X \times L^2) \div L^3 = (|\mathbf{v}| \times \cos\theta_X) \div L$ (min^{-1}). There is an analogous first-order rate constant for a particle leaving the cell due to advective flow to the neighboring cell in front (or back) and the neighboring cell above (or below).

The conversion of the eddy diffusivity coefficient D (m^2 min^{-1}) for each cell (node) into a first-order rate constant would follow the method used for the Level I model (Nicas and Nazaroff, 2004). Where λ_D (min^{-1}) denotes the rate constant for a particle leaving a cell due to turbulent eddy diffusion: $\lambda_D = (6\ D) \div L^2$. The first-order rate at which a particle is carried to a given neighboring cell (say, the cell on the right) by turbulent eddy diffusion is $1/6 \times \lambda_D$.

Integration of the CFD and Markov chain modeling approaches would be a collaborative effort among the group at UC-Berkeley and Dr. Charles Haas at Drexel University. Dr. Haas conducts research using CFD techniques, and would generate room air velocity and turbulent diffusivity fields for scenarios of interest.

Aim 3 – The performance of the Level I Markov chain model would be tested against the Level II model as a means to explore exposure intensity of building occupants to airborne BAC. An important practical question in developing and applying inhalation exposure models to BAC is the extent to which detailed knowledge of the airflow conditions in any particular space is essential for understanding exposure.

When considering different levels of detail in the treatment, at one end of the spectrum is the well-mixed model construct, which treats the particle concentration as uniform throughout the room, and at the other end is CFD, which predicts the spatial distribution of particle concentrations. The well-mixed construct is mathematically simple, but cannot describe the observation that exposure intensity increases with proximity to the emission source. The detail provided by CFD captures spatial variability in exposure intensity, but at a steep computational cost; further, exact prediction of particle exposure is beyond the current state-of-the-art in airflow simulation. What is not yet clear is how detailed a description must be produced for a microbial risk assessment. Interest in practical application of exposure modeling tools argues for careful exploration of the modeling domain between the well-mixed representation, and models based on the fully space-and-time resolved air velocity fields.

Experimental Approach At UC-Berkeley, we would undertake several case studies in which we would simulate exposure intensity fields using the Markov chain model, but with different levels of detail in the treatment of the air flow field. Either from the literature and/or in collaboration with Dr. Haas at Drexel University, the group at UC-Berkeley would obtain a detailed airflow simulation of a realistic indoor space. We anticipate that the simulation would employ CFD, probably based on the well-established k-epsilon model of turbulent flow. We would run Level II simulations of the Markov chain model using these airflow fields as input. We would also run Level I simulations using simpler representations of the airflow conditions. We would explore how the properties of the exposure intensity field vary between these two types of simulations.

Objective 6: Measure the resuspension of particle-associated BAC in a test room or chamber

The aim is to assess the potential for resuspending into room air particle-associated BAC which are present on room surfaces. The particles to which BAC are attached are traditionally termed fomites. Given that the pathogen remains viable on surfaces for a sufficient duration, resuspension can lead to inhalation infection of room occupants in the absence of an active BAC release source such as an aerosol generating device or an infectious individual. Resuspension of settled anthrax spores was documented in the Hart Senate Office building bioterrorist attack of Fall 2001.

Experimental Approach. At UC-Berkeley, experiments would initially be conducted using fluorescein-labeled particles. Several particle matrices would be examined, for example, an artificial respiratory fluid (as a surrogate for pathogens in respiratory fluid particles expelled by individuals with respiratory tract infections), tap water (as a surrogate for pathogens that can be aerosolized from tap water), soil (as a surrogate for pathogens carried by soil particles due to ambient release of the pathogen) and fibers (as a surrogate for pathogens carried on fibers that are shed from contaminated clothing). The particles would be released as aerosol inside a test chamber to attain a fairly uniform deposition over the floor; the amount of fluorescein deposited would be assayed from samples of collection media on the chamber floor (and on wall surfaces). Next, air movement inside the chamber would be induced using one or more fans, and perhaps

by moving an object inside the chamber. Air sampling would be conducted at locations inside the chamber during different periods of the duration of air motion. Exhaust air from the chamber would be passed through a separate filter to collect resuspended particles not collected by the within-chamber air samples. Once the induced air motion is terminated, samples of collection media on the floor (and walls) would be analyzed for fluorescein mass. In theory, the estimated fluorescein mass originally deposited on the chamber surfaces (denoted mass Dep) should equal the fluorescein mass collected on the within-chamber and exhaust air samples (denoted collectively as mass Air) plus the flourescein mass remaining on chamber surfaces (denoted mass Rem), or Dep = Air + Rem. The estimated percent of particle mass resuspended is (Air ÷ Dep) × 100%.

We would investigate the influence of several factors, which are expected *a priori* to affect the extent of particle resuspension. These factors include the type of surface (e.g., cement, stainless steel, linoleum, wood, carpet), the size of the particles deposited, the electrostatic charge on the particles, the absolute humidity of the air, and the intensity of air motion. The results with fluorescein-labeled particles would be confirmed with surrogate BAC particles developed at the University of Arizona, Northern Arizona University, and Michigan State University.

Objective 7: Determine the Particle Size Distribution of Respiratory Aerosol-

A major threat of BAC is posed by secondary infections in which diseased individuals become vectors for infecting others. The size and number of respiratory particles emitted by human subjects during ordinary activities is a key aspect affecting the probability of secondary infection. As reviewed in a recent paper (Nicas, Nazaroff and Hubbard, 2004), only a few experiments have been conducted to measure the size distribution of respiratory particle emissions, and the results from these experiments are not consistent with one another. Additional experimental work is needed to measure the size distribution of human respiratory particle emissions.

Experimental Approach At UC-Berkeley, we would conduct laboratory-based experiments to measure the respiratory droplet size distribution emitted both from healthy subjects and from those with respiratory infection. The first phase of this project would be method development and testing. The second phase would involve applying the method to collect data from several subjects in different emission modes.

Two promising measurement approaches are available. In the first approach, we envision that a test subject would be placed in a small test room supplied with particle-free air (achieved by means of HEPA filtration). The subject would wear low-particle clothing, such as is used in semiconductor manufacturing. We envision that the subject's expelled respiratory aerosol would enter a room air stream flowing at a known volumetric rate in uniform fashion through a cylindrical structure; the intent of the structure is to contain the aerosol and present it to one or more sampling devices. An aerodynamic particle sizer is capable of measuring size-resolved particle number concentrations over the range 0.5-10 μm in diameter would be positioned in the air stream a short distance downstream from the entry point of the aerosol. Emission events would be triggered, and the number of particles emitted and their size distribution would be inferred from the sampling data for each event. In the second approach, a small quantity of a safe but easily measured dye would be introduced into the subject's mouth; a similar dye technique was utilized in two early studies of the size distribution of respiratory aerosol (Duguid, 1946; Louden and Roberts, 1967) The emissions protocol would be similar to that used in the first procedure. Sampling would be done using a cascade impactor, and the amount of dye deposited on each stage would be related to emissions of particles in that particular size range.

We propose to make measurements using six subjects initially – three healthy subjects and three subjects with respiratory infection. The modes of emission to be studied would include coughing, sneezing, and talking.

Project Management Dr. Gerba will be the lead investigator for this project. He will coordinate the efforts between the groups involved in the exposure assessment. He will also ensure that the data produced is in a format that can be used by the other projects on-going in the center (risk assessment modeling). UA (Gerba) and NAU (Keim) will be responsible for surrogate development and assessment. The UA team will include Dr. Gerba Dr Choi and Dr. Ian Pepper, as a co-investigator (UA) and they will also be responsible for fate and transport by fomites and water systems, with in-put from the NAU group. Dr. Choi will be responsible for the neural network modeling. Dr. Pepper will be responsible for the management of the facilities at the "Water Village" during the planned studies on water systems and release of surrogates into buildings. The UCB team includes principal investigator Dr. Nicas and co-investigators Dr. Nazaroff and Dr. Hubbard, who will be responsible for aerosol modeling and resuspension from fomites. The MSU team (Dr. Hashsham and Dr. Rose) will lead the efforts on the detection systems with input from UA and NAU.

Facilities **University of Arizona** has 2,500 sq. ft. of laboratory space with areas for bacteriological, virological, and parasite analyses of water, soil, food and fomites, meeting all BL-2 standards for pathogens, cell culture and molecular biology. The Heat and Mass Transfer Laboratory of Dr. Choi is equipped with data loggers and various sensors for real-time, remote (using RF and cell phone modem) monitoring in aquatic systems for field scale experiments, water-related control devices, pumps, and testing and data acquisition units. A workstation is dedicated to running MATLAB with Neural Network Toolbox. A computation fluid dynamics package is also available for the proposed research activities. The Water Village of the Environmental Research Laboratory (ERL) has separate buildings containing analytical laboratories (for soil, fomite, and water chemical and microbial analysis), green houses, aquaculture facilities, meeting facilities, and offices. A drinking water distribution system is under construction to four existing dwellings, which will serve to assess the detection and fate of biological and chemical agents in distribution systems; as a model community for the testing and evaluation of real time monitoring of intentional chemical and biological intrusions, the dispersion and clean up of BAC in the distribution system and within buildings. It will contain sensors for water quality (pH, temperature, dissolved solids, etc) throughout the network for continuous monitoring. It will also be possible to change the water at various points in the distribution system and remove selection of piping for testing and observation. Water use in the homes (kitchen tap, showers) will mimic that in actual family of four homes. It will also be possible to do aerosol release in these homes to assess dispersion and potential success of clean-up efforts.

Michigan State University. Facilities available include three automatic in situ biochip hybridization stations, a glass slide arrayer, Axon Instruments GenePix 4000A and 4000B laser scanners, Gel documentation system, laminar flow hoods, and GeneSpring Data Analysis Software, Array Designer probe design software. Drs. Hashsham and Rose also have laboratory space in the Center for Microbial Ecology which is well equipped with a full range of microbiological and molecular biological equipment including fluorescent microscopy with image processing, shakers, anaerobic glove box, Hungate-type anaerobic gassing apparatus, 3 ultra-centrifuges, electrophoresis systems, and thermocyclers. The laboratory also has several

GC's, HPLC's, and a capillary electrophoresis unit with laser-induced fluorescence detector. The MSU Genomic Technology and Support Facility is in the adjacent building and has 3 high throughput sequencers and associated robotics, software and staff. Also next door are the Macromolecular Synthesis Facility (for primer synthesis, peptide sequencing), the NIH-supported Regional Mass Spectrometry Laboratory, and the MSU Center for Electron Optics with a range of electron microscopes and confocal laser scanning microscopes with 3-D image reconstruction.

University of California at Berkeley. The Aerosol Research Laboratory, Davis Hall, of Dr. William Nazaroff is equipped with aerosol-generating equipment (vibrating orifice aerosol generator, nebulizer with electrostatic classifier) that can produce polydisperse or monodisperse particles of known materials. There is controlled deposition test chamber (2 m^3). The laboratory also contains equipment for sampling and analysis of fluorescein-labeled, both sampled from air and deposited on surfaces. Dr. Nicas and Dr. McKone have fully equipped offices on campus with Internet connections. Dr. Nicas' office has two Dell work stations, one of which has an Intel Xeon processor and 4 GB RAM, and is dedicated to running MATLAB® code implementing Markov chain models.

Northern Arizona University. The Keim Genetics Laboratory (KGL) occupies ca. 7,000 square feet of wet bench and office space. The KGL will move into new, larger facilities (~10,000 square feet) in the Applied Research and Development Building early 2006.Current equipment includes Pulse Field Gel Electrophoresis gear, a gel documentation system, several DNA Sequencers, thermocyclers , a Packard Robotic Platform for assembling PCR reactions. The KGL has a CDC Select Agents permit (CDC Permit# C20031122-0107) and USDA permits for possession, use, interstate transport (USDA PERMIT# 50870), and importation (USDA PERMIT # 47449) of live *Bacillus anthracis, Yersinia pestis, Burkholderia pseudomallei, B. mallei*, and attenuated *Francisella tularensis.* The laboratory has high security for protecting these agents that will not be detailed here to protect this security. The select agent suite is a closed and secured room of ca. 500 square feet, which is under negative air pressure. Inside the suite, there are two class IIA/B3 biosafety cabinets for handling live agents. Following its move to a new building, the KGL will have a BSL-3 suite in addition to a BSL-2 suite.

Project Time LIne	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
Development of BAC surrogates	**X**					
Validation of detection methods						
Assessment of best methods	**X**	**X**	**X**	**X**	**X**	**X**
Surrogate methods identification	**X**	**X**				
Sample needs for risk models			**X**	**X**		
Gene sequences as a tool in risk assessment				**X**	**X**	**X**
Water Systems modeling						
Model development and design	**X**	**X**				
Field studies (Water Village)		**X**	**X**	**X**		
Fomite Studies and modeling				**X**	**X**	**X**
Aerosol studies						
Particle fate and transport in a room	**X**	**X**	**X**			
Resuspension of particles				**X**	**X**	
Determine particle size distribution					**X**	**X**

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Project II. Infectious Disease Models for Assessing Microbial Risks and Developing Control Strategies

Objectives

Microbial risk for transmissible infections has distinct individual and population components. The release of pathogens into the environment may have higher or lower direct effects on individuals exposed to the contaminated environment depending upon how much transmission is occurring via other routes and stimulating immunity. Pathogens in the environment also may have higher or lower indirect effects depending on whether the secondary cases transmitted from the index cases generate sustained chains of transmission. Standard risk model estimates are obtained by only considering the direct risks. If an analysis of transmission through the population is not part of the risk assessment, no generalizable conclusions regarding risk can be made from a direct effect estimate. Accounting for the changing levels of direct and indirect risks requires information at the population level on who is infectious, who is susceptible, and who is immune. This changes over time and will depend on a number of factors including levels of environmental contamination and patterns of contact between individuals and between individuals and the environment. Thus predictions regarding such changes are a crucial element of microbial risk assessment for transmissible infections that are not at all a part of risk assessment for non-transmissible infections. To accurately characterize microbial risk, therefore, requires a model that: 1) is dynamic, nonlinear, can account for the heterogeneous nature of the disease process within individuals as well as heterogeneous patterns of contact between individuals; 2) encompasses both human and environmental contributions to transmission; 3) integrates control potential and control resource limitations into the assessment of risk; and 4) can be used to assess the validity of inferences regarding the consequences of bioterrorist and infection control actions. Specifically, we propose to develop a methodology that provides explicit links between the models of environmental exposure and models of the disease process, focusing on how heterogeneity will impact risk. This methodology will be used to integrate environmental and dose-response data and to aid in: a) early detection of outbreaks; b) planning for both short- and long-term control efforts, and c) setting research agendas.

A bioterrorist incident, as with all outbreaks, is highly dynamic. There are many temporal aspects of an outbreak that make it dynamic. First, a point-source exposure in a bioterrorist incident will generate cases that occur over time. Second, exposure conditions may change over this same time period altering the risk from future exposure events. And third, for transmissible pathogens, individuals infected from the initial point-source attack will put others at risk. Transmission models have been used extensively to examine many infectious disease processes. There has been much less work in developing transmission models that explicitly model the environmental processes of pathogens, an critical component of risk assessment. An exception to this is in the area of water quality where water quality measurements have been integrated into transmission models to estimate risk (Chick et al. 2002, Eisenberg et al. In press, Soller et al. 2003). An important component of this research will be to develop appropriate infection models that can address both large and small scale outbreaks, that can estimate both immediate point source risks as well as longer term risk conditions due to the spread of infection, and that can examine pathogens that can be transmitted via surfaces, hands, air, food, and water.

As with all disease processes, the patterns of disease will be heterogeneous in space and time. The incorporation of this heterogeneity is important for any adequate estimation of risk but

it is especially important for transmissible infections where different contact patterns between population segments with different individual risks can dramatically change both the direct and indirect effects from an environmental exposure. There are a number of sources of heterogeneity. Some sources are clearly associated with heterogeneity in exposure. However others are functions of heterogeneity amongst the individuals or within the population that is exposed. Another important component of this research, therefore, will be to use our methodology and risk models to ascertain the impact of different sources of heterogeneity on risk as well as the impact of contact patterns. Some of these sources are focused at individual-level dose response relationships such as: variability in the intrinsic infectivity and virulence of the infectious agents (including potential alterations from "weaponization" of organisms of concern); or variability in the response of individuals to the infectious agent (and modification by intrinsic extrinsic factors influencing susceptibility); and differences in severity and duration of outcomes resulting from exposure. Other sources are focused at the population level such as: differences in susceptibility to the bioterrorist agent due to different contact patterns that have circulated infection and thus stimulated immunity differently; differences in exposure to infected individuals in the contagious state (presence of "super-spreaders" or failures of quarantine or containment); differences in environmental exposures.

It is generally envisioned that bioterrorist attacks will occur through the environment. Risk assessment models, therefore, must have an explicit description of the exposure pathways that are relevant for bio-terrorist activities. The release of a pathogen can occur via different media, such as: water, through post-treatment contamination; food through manufacturing or farm contamination; air through aerosol release or circulating infectious individuals, and surfaces that might be contaminated in a variety of ways including mailed letters as occurred with anthrax. The value of environmental measurements of microbial contamination is not just with regard to measurement of original sources of agent from a bioterrorist. Secondary transmission from human to human can also occur via surfaces, air, water, food and in addition via hands. Measurements of microbial environmental contamination have not as yet been used to help model the spread of infection through populations. We will devise methods where such measurements contribute to understanding how the transmission system works and what actions will best bring transmission under control.

To create exposure sub-processes within risk assessment models requires specific information on the fate and transport of microorganisms. Although exposure assessment is a central part of microbial risk assessments for food and water, there has been less work linking comprehensive exposure models with transmission models. To be relevant for examining risks associated with bioterrorist events, microbial risk assessment needs to be generalized to a broader set of exposure/disease scenarios. To this end we plan to develop important linkages to the exposure research group in our Center. Specifically, the risk assessment methodology will be used to help design the most effective environmental sampling strategies, including surface, air, human hand, water, and food. It is not obvious whether very frequent measurements at a small number of places will contribute more to controlling transmission risk than less frequent measurements at more spots. Or whether using environmental monitoring techniques that have a lower detection level but can only be used at fewer sites, due to higher costs per sample, would provide better information for the risk estimates, than less costly techniques (with higher detection levels) that can be used to produce more sample points. These different strategies may require different technologies. By defining what strategies contribute most to infection control,

we will help set research and development priorities for developing technology needed for the most effective strategies.

Based on the importance of viewing risk to bio-terrorist attacks as a dynamic, heterogeneous, and environmentally mediated process, we propose the following specific objectives:

- To develop appropriate transmission models that are dynamic and provide spatially explicit details of infection spread through populations. Specifically, the models will allow for individuals to spend different amounts of time at different places, to contaminate the environment and in turn to acquire infection from the environment. This development process will involve construction and analyses of complementary deterministic and stochastic models of infection transmission where the media by which infection reaches from one person to another is explicitly modeled.
- To use existing data sets to identify parameters of interest including secondary transmission rates, contact patterns, and dose response functions. To this end, outbreak data and other epidemiological studies will be used to identify parameters associated with the infection process while environmental microbiology data will be used to identify the fate and transport processes. Heterogeneous factors will be characterized.
- To use the models developed in the previous objectives to analyze different outbreak scenarios associated with local contamination, and to examine the efficacy of local control actions at different environmental points or within different population groups. And to use these models as a testbed for developing and evaluating sampling and analysis methods that can be used under the emergency conditions of a bioterrorist related outbreak, as a guide for resource allocation in the face of uncertainties related to the natural history and transmissibility of infection and persistence of the agent in the environment.

We plan to look at a variety of pathogens that are on the Class A and B lists of bioterrorist agents and are transmissible from human to human. Specifically, we propose to examine a group of pathogens, such as small pox and noroviruses for which a reasonable amount of data exists, as well as a group of pathogens, such as Ebola, in which few data exist. In addition, we propose to examine other pathogens such as influenza (which is on the class C list) and SARS as surrogates. The SARS coronavirus is has characteristics of an ideal bioterrorist agent. It has proven its ability to generate panic, dramatically drain resources, and disrupt economic activity in diverse modern societies. It has a basic reproduction number similar to that of smallpox but its shorter incubation period and consequent lack of potential for post-exposure vaccination make it less controllable.

Approach

Developing Transmission Models

We will construct models of transmission through water and through droplet spread involving direct contact, fomites, and surfaces at environmental sites. These models will include descriptions of the pathogen fate and transport processes within the environment. The goal of this modeling process is to obtain a balance such that models have sufficient detail to capture the complexity of the fate and transport processes as well as sufficient detail to evaluate the robustness of model based inferences to unknown aspects of those details, without being overly

computationally intensive or difficult to interpret. The level of detail in a model largely depends on the types of control measures that are being considered. To examine the effect of decontamination at a particular site, for example, one needs to understand not only the patterns of contact with that environmental site but also the patterns of contact among people.

Rather than seek a generally utilizable model for any purpose, we will develop a flexible hierarchy of models that can be adapted to work in concert to address specific questions. In their simpler forms these models will provide general insights as to how to prepare for bioterrorist incidents and in their more realistic forms will be modifiable to address specific scenarios before or during an emergency. By constructing a hierarchy of models, we will improve both the theoretical basis for model construction and analysis and the modeling tools to apply that theory under emergency conditions.

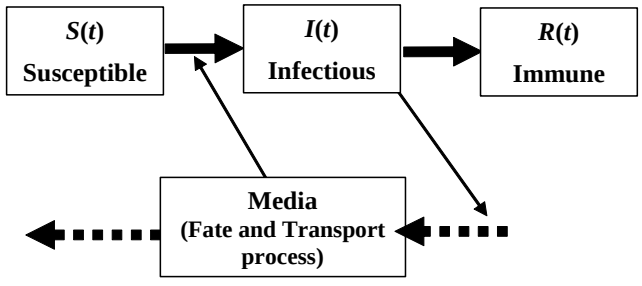
General aspects of model analysis

This proposal benefits from complimentary approaches pursued by Koopman and Eisenberg. Both will focus on infections spread via the environment and the role of different strategies in controlling a bioterrorist initiated epidemic. Koopman's work will focus on environmental aspects of droplet and airborne spread infection and the role of decontamination or establishing barriers to environmental exposures, while Eisenberg's work will focus on environmental aspects of waterborne transmission and the role of water-based control strategies. One important focus of this work will be to pursue robust assessment that improves inferences about needed control actions by assessing how assumptions about the transmission system affect those inferences. There are always unknown aspects of the transmission system about which one needs to make control inferences. Our strategy is to formulate models with parameters expressing those assumptions rather than bury those parameters with inappropriate model simplifications whenever we judge that unknown aspects of the transmission system might influence the inferences we need to make. An example of the type of robustness assessment to be pursued is an analysis of control measure effects in the Beijing SARS epidemic, which we have just submitted for review. In this study we examined the benefits of contact tracing in the control of the epidemic. This robust assessment technique is described in more detail in Section 2.2. Another result of our analysis was the demonstration of how important measurements of exposure behavior in the general population are for making inferences about the effectiveness of control efforts. This finding should stimulate the establishment of surveillance systems that involve collecting routinely tabulated data on activities that increase contact among individuals, such as attendance figures at public events or sales figures that reflect public exposure during shopping. For decisions about decontamination, the work to be performed under this grant would highlight what type of data would improve the robustness of decisions about when and where to decontaminate.

We will also focus on attaining inference on control action based on known processes that are highly uncertain. An example of this type of assessment is illustrated in previous work by Eisenberg et al, in which they examined optimal control strategies for recreational water exposure (Eisenberg et al. 2002, Eisenberg et al. 1996). An analysis of the risks associated with swimming suggested that the optimal decision given the choice between localized control by limiting swimming exposure and a more centralized control of improving water treatment depended heavily on the rate at which infected swimmers shed pathogens into the water. The analysis further stipulated to what degree this rate need to be identified in order to attain a given level of confidence in the decision of one control option over the other.

To attain these goals, we will relate standard deterministic compartmental models that assume instantaneous contacts with instantaneously thorough mixing after contact to deterministic models that specify media contamination, agent survival and transport in media, and media uptake. We will in turn relate these to stochastic compartmental models that do not make the assumptions of infinite population divisibility in each compartment. These in turn will be related to stochastic individual event history models that follow individuals rather than compartment totals and thus provide for greater degrees of heterogeneity. Our overall goal in the model development phase will be to relate models of differing form that make different assumptions as well as models of similar form that specify different levels of realistic details affecting risk. A rationale and framework for such model interdigitation has been presented elsewhere (Koopman 2004, Koopman et al. 2001).

Relating models of different form and degrees of complexity serves two purposes. First, it facilitates robustness assessment. Second, it facilitates model fitting to infection outcome and environmental contamination patterns. As an example of using multiple models, consider the problem of deciding on key environmental transmission sites for droplet spread infections like SARS where decontamination actions might be justified. As an initial step, deterministic model analysis can be used to gain insights into the roles that different sites play in the transmission system, which may narrow down a decision to decontaminate. One must be aware, however, that those insights may not be robust to realistic violation of the infinitely divisible population assumptions of deterministic models. If one is familiar with the expected effects of a transition from deterministic to stochastic models, one can better use the deterministic models as a first step in an analysis that narrows down a decision to decontaminate. Then one can see whether the effects of such decontamination change enough given the transition from deterministic to stochastic models so that the decision to decontaminate is changed. As a second step a more detailed issue may be to decide whether to choose localities where environmental contamination exposes large numbers of individuals or to focus control on different sites that might act to disseminate infection to other sites. For this step a stochastic model becomes essential because deterministic models miss important aspects of the infection dissemination that are captured by stochastic models (Koopman et al. 2002).



Integrating transmission models with environmental models

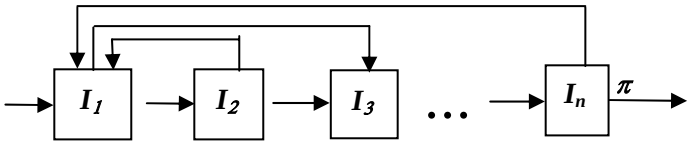
One major strategy in our model construction will be to designate different environmental sites where transmission can take place. This serves two major purposes. First, it establishes the contact patterns that circulate infectious agents in the population and stimulate immunity. Second, it provides specific human environment interaction sites or environmental agent transport sites where the environmental models can be integrated into the population transmission models and where environmental measurements of agent levels can serve to inform model conformation and parameter estimates.

For any particular mode of transmission we will model the media, such as air, water, surfaces, etc that either bioterrorists or infected individuals might contaminate. The contamination of the media, the agent survival and transport in the media, and the uptake of the agent are all parts of the model. Parameters specific to contamination and uptake processes must

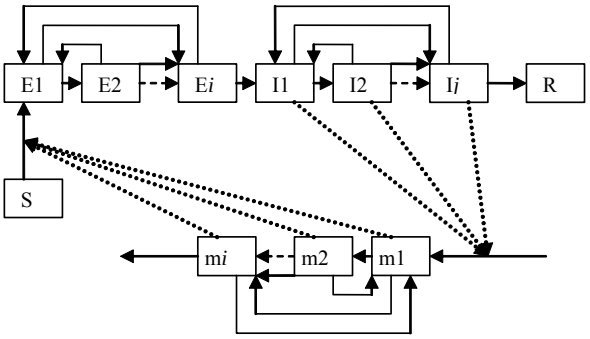
be specified in exposure models. The simplest model form possible is illustrated in the adjacent compartmental model figure. This model tracks the number of individuals in different disease states. Specifically, there are three disease states: **S**, represent those who are susceptible to disease; **I,** represent those who are infectious; and **R**, represent those who are non-infectious and protected from becoming reinfected. In addition there is at least one state that accounts for the concentration of pathogens in the environmental media. The thick solid lines represent the movement of individuals from one disease state to another. The thick dashed lines represent movement of living pathogens into and out of the media. The thin lines represent influences on these flows. The more infectious individuals there are, the higher will be the flow of agents into the media and the more media contamination with live agents, the higher will be the flow from susceptible to infected individuals. In this sketch all details of the natural history of infection and of agent survival or transport are ignored. The models we will develop will include details that specify living and non-living agents in the media. Measurement of non-living agents can be just as or more helpful in assessing venue specific contamination rates from infectious individuals as measurements of live agents. Only living agents affect infection risk. Thus measurements of both live and dead organisms in the environment will help specify the models but both might not be needed, depending on the results of robustness assessment for the particular decisions being addressed.

Note that compartmental models that incorporate the transmission media do relax several unrealistic assumptions of standard compartmental models of infection; e.g., they do not assume that contact is symmetric but rather allow for directional transmission from someone who is first at a site to someone who comes later. Similarly, they do not assume that contact is an instantaneous process of individuals bumping into each other but rather incorporate the time that an individual is at a site depositing and or acquiring agent from the media. This formulation also replaces the standard assumption of thorough and instantaneous mixing after a contact with the assumption of even contamination of media at a locality. Eisenberg and Koopman have addressed these modeling issues in risk asessment studies focused on water (Chick et al. 2001, Chick et al. 2002, Eisenberg et al. 2004, Eisenberg et al. In press, Soller et al. 2003). The goal in this proposal is to generalize these concepts to other media important in pathogen transmission and expand them in ways that enable environmental contamination measurements contribute more to the conformation of transmission system models.

One important extension to this model will be to capture temporal patterns for incubation and contagious periods. We will examine different approaches to capturing these patterns using different distributional forms. To retain an ordinary differential equation format consistent with our deterministic compartmental models, we will employ a strategy of sequential cycling of compartments. It is possible to approximate most shapes using sequential compartments with different recirculation patterns through the sequence. In the below diagram the contagious process is assumed to move through a series of compartments with a fraction of population skipping certain processes and other population fractions reverting back to previous processes. A simplified version of this approach was used in previous modeling studies (Eisenberg et al. In press, Eisenberg et al. 1998). Alternatively, when we transit to discrete individual model forms, we will also examine the use of functional distribution forms as in Gupta and Haas (Gupta and Haas 2004). When inferences are shown to be robust to incubation period distribution forms, we will of course use the most computationally efficient forms.



Modeling environmental fate and transport



Consistent with our philosophy of relating simpler and more complex models and models that make contrasting assumptions, we will assess the level of detail in the models developed by the exposure group that is necessary to make appropriate control inferences. We will do this initially by capturing the patterns of output from the exposure group models in a compartmental model analysis form. As with incubation and contagious period, temporal patterns for agent survival in the environment may assume different shapes as a result of the exposure models developed, and it is possible to approximate most shapes using sequential compartments with different recirculation patterns through the sequence. We will use this strategy to assess the importance for control inferences of any model refinements in these distributions developed by the exposure group. The attached figure gives a schematic for such a compartmental analysis approach. If the shapes make a difference, then we will proceed to integrate the actual exposure group models.

As with the previous model discussed above, the dashed arrows in the figures connecting media boxes in the adjacent figure represent the influence of infectious individuals on environmental contamination and the influence of environmental contamination on infection risks. Transport of media is an issue for water where the sites of contamination and uptake may differ. Transport will be addressed by a set of compartment flows orthogonal to time. A related issue is when surface contamination results ultimately in aerosol transmission. Many years ago Koopman demonstrated the importance of this phenomenon for diphtheria transmission (Koopman and Campbell 1975). Environmental measurements of diphtheria contamination were found to be far greater in the presence of infected individuals with skin lesions. In turn, respiratory infection risk was found to be greater in the presence of the environmental contamination. The Amoy Gardens episode in Hong Kong(Lau et al. 2004, Yu et al. 2004), aircraft transmissions(Olsen et al. 2003) and the laboratory transmissions that have been documented(Orellana 2004) illustrate the potential importance of such phenomena for SARS. The exposure group will have primary responsibility for developing environmental models that account for this route of transmission. A double layer of media where the surface media feeds into the aerosol media would be a simple way to approach this situation. One utility of such a double media model may be that decontamination measures might be cheaper if they are directed to preventing aerosolization rather than to complete elimination of viable organisms.

Contact pattern generation

To complete the description of transmission, contact patterns of individuals must also be incorporated into the transmission models. All movement to different sites where the time spent at a site is relatively short will be modeled in a statistical mechanics framework where fractions of each individual are continuously at each site. Only when actual residence migration occurs, such as when people move out of an epidemic area, will migration be addressed. By specifying the amount of time that individuals with different characteristics spend at each site, one generates contact patterns that may vary from assortative to proportionate mixing in as many dimensions as there are environmental sites. This framework cannot incorporate dissassortative contact patterns such as those generated by medical personnel directing their contacts to patients. We would only address such contacts if and when we see the need for a specific robustness assessment that takes into account disassortative contacts. We would only do so within the discrete individual stochastic models.

Environmental sites may be described as abstractly as broad areas of a city and as specifically as specific rooms in specific buildings. Hospitals in particular may be important sites to model since special contamination prevention and decontamination actions are often taken there. The level of detail needed for social structure defined by environmental site attendance will vary depending upon the control measures being evaluated. For decontamination, broad sites may be adequate. For quarantine, local sites such as homes may be needed.

Accounting for heterogeneity in the infection process

Variability in transmission processes often drive risk. For example, water quality data collected in the source and finished waters suggest that often there are no pathogens, while occasionally the concentrations are quite high. This suggests that infection occurs in the form of outbreaks. When the magnitude of a cluster of cases is small and below detection level it will go unnoticed. The sum of these small outbreaks are often captured in surveillance as an aggregate and viewed as the endemic level. Only when the magnitude of a cluster of cases is above a threshold does it get categorized as an outbreak. Likewise, infectious individuals often recover without transmitting the pathogen to anyone. Occasionally, however, there are individuals that are labeled “super-spreaders” in that they will transmit the pathogen to a large number of individuals. This was well documented in the SARS epidemic (Shen et al. 2004). Other sources of heterogeneity also exist such as differential susceptibility. Susceptibility of individuals may vary by different demographic factors such as age or immune status. Each of these demographic groups will have different dose-response relationships.

We will construct models that include these heterogeneities. We will explore different model structures to handle exposure variability, contact patterns, and dose-response. Specifically, we will be interested in examining the impact of each of these types of heterogeneities on risk estimates.

Model Parameterization and Identifiability

To apply the models developed as described in Section 2.1 in a risk assessment requires a process of identifying values for parameters used in a given model. For some parameters this may be a simple process of extracting data from the literature, since all model parameters will have some sort biological or physical interpretation. For example, either a point value or distributional estimate for incubation period could come straight from a literature review

(incorporating a distribution may also have structural implications for the model as discussed in Section 2.1). Alternatively, outcome data (either incidence or environmental) may be used to identify parameters statistically. Standard statistical techniques, however, are not generally useful for fitting the types of models discussed in Section 2.1. Unlike standard statistical models whose primary aim is a succinct description of the stochastic relationship between observed random variables, population dynamic models are mechanistic representations of complex population processes. As such, the model parameters are easily interpretable and scientifically relevant, however the relationship between these parameters and the model output can be complex. The overall objective of tasks discussed in this section is to first create a database of information important to parameterizing and identifying models, and second to examine a variety of statistical techniques that address the problems associated with highly parameterized nonlinear models.

Developing a database of relevant epidemiological and environmental data

Although most of our transmission related risk assessment will focus on noroviruses and SARS, we plan to develop a database with a wider set of bioterrorist relevant pathogens. We will include a variety of bacterial pathogens, such as *Bacillus anthracis*, *Yersina pestis*, and *Francisella tularencis*, as well as a variety of viral pathogens, such as pox viruses, Hepatitis A, and Ebola. For all of these pathogens, a literature search will be conducted to compile: 1) information on outbreaks and prospective epidemiology studies, and 2) information on important biological and environmental processes. This information on outbreaks will be gathered by taking advantage of previous work conducted by the CDC and EPA. A literature search using the standard bibliographic databases will be next conducted to obtain any outbreaks not compiled by the CDC or EPA. To gather information on important biological and environmental processes we will begin by integrating databases already developed from previous projects by investigators of this specific project module (Eisenberg, Koopman), as well as investigators from the Center (Nicas, Haas). Again, a literature search will follow to collect any information missed by previous data gathering activities or that have been published in the last few years. Other investigators from the Center (Keim, Rose, Haas, Nicas) will participate in this database development task. The integration among projects will be particularly facilitated by the knowledge management depository to be developed at Drexel for CAMRA.

Statistical techniques for examining control strategies

In parallel with these database activities, we plan to examine, and modify if necessary, the following statistical approaches: robust assessment using least squares, profile likelihood, Bayesian, and a regional sensitivity analysis

Robust assessment using least squares fitting

For nonlinear system parameter estimation, it is quite difficult to assure that the least squares parameter search reaches a global minimum. This is especially the case for complex models with many parameters to fit. To address this issue, we haven taken an approach that seeks to specify diverse parameter sets that fit the data and to evaluate decisions across all of the parameter sets that fit the data. An example of this is our SARS analysis, in which we established a close collaboration with the people who controlled the Beijing SARS epidemic. We extracted a set of 25 data points from the more that 50 specific research files they have established on epidemic data. The data showed that less than 20% of cases were diagnosed

through tracing, and that the average time between symptom onset and diagnosis fell from 6.3 days early in the epidemic to less than 2 days at the end. These data suggest that improved diagnosis without tracing did much more to control the epidemic than tracing. But our unique analyses and robustness assessments showed the opposite to be true. Our model captured the dynamics of: diagnosis with isolation; contact tracing with quarantine; contact rate reduction from public behavior change and public health actions; and diagnosis of noncoronavirus atypical pneumonia cases as SARS. To make inferences about control actions we developed a robustness assessment strategy. For each of the 16 model parameters we found the extreme values that would still allow for the average data point generated by the model to be within 20% of the observed values when all of the other parameters were allowed to vary. We then examined several intermediate values using different initial guess values in the least squares minimization algorithms. For each of 160 fits found, we examined the effect of eliminating either the improved diagnosis program or the tracing program. Thus we have extensive robustness assessments on our inferences about these two effects. In each of the 160 fits, eliminating tracing had the bigger effect. On average the difference was five fold. The reason for this surprising effect was readily demonstrated by our model analysis to be that the nonlinear dynamics of tracing amplified the effects of diagnosis without tracing while there was no such effect in the opposite direction. Analysis also demonstrated that we should have considerable power for analysis of other control actions in Beijing, such as the extensive decontamination efforts they undertook, once the sera on the 2521 probable cases weed out false positive cases.

Profile Likelihood

Another way around the problems associated with highly parameterized models is the profile likelihood approach (Brookhart et al. 2002). In this approach maximum likelihood estimates are obtained by fixing a set of parameters of interest over a range of values and then maximizing the full likelihood over the remaining "nuisance" parameters. The likelihood ratio test provides a reference value for evaluating particular parameter sets. Those sets with profile likelihood values above the reference value are considered reasonable and are included in the confidence interval while those below are rejected as implausible. This approach leads to robust confidence intervals. The computational advantages are derived from being able to fix parameters that are either interesting or troublesome, so that the remaining optimization problem is simplified. Prior information about nuisance parameters (e.g. duration of infection) can be incorporated into the estimation approach by constraining the particular parameter to a range of realistic values. In analyzing the *Cryptosporidium* outbreak in Milwaukee, we were able to use the parameter estimates obtained using this profile likelihood approach to make predictions on differing causes of the outbreak and potential control efforts to minimize the chances of other outbreaks like this one occurring (Eisenberg et al. In press).

Bayesian technique

To examine attributable risks, MLE techniques like those described above are limited for obtaining inference on attributable risk estimates. Bayesian techniques provide an approach to estimate the multivariate posterior distribution of the model parameters. For every combination of previously identified profiled parameters, the resulting parameters can be estimated using a Monte Carlo Markov Chain (MCMC) technique. To handle the potential colinearities (non-identifiabilities) of parameter estimates in the data a novel two-step approach to the Metropolis-

Hasting procedure (Metropolis and Hasting, 1971) can be used to generate samples from the posterior parameter distribution (AJE). First, we created a dense grid of the parameter subspace defined by the parameters over which we profile. For each point in this multi-dimensional grid, we run the MH algorithm over the remaining parameters to generate a posterior distribution assuming the parameters defining the grid are fixed. When this procedure is finished, the result is a sample of all parameters and the associated likelihood. Finally, we employ a random MH algorithm that uses as trial parameter sets, rows from this data set. After this second step is performed, the result is a sample of the multivariate posterior distribution of all the parameters. This procedure was used to establish the contribution of secondary transmission in the Milwaukee outbreak (Eisenberg et al. In press).

Regional sensitivity analysis

Traditional likelihood approach requires incidence data as well as a measure of uncertainty of those data. An alternative approach is based on the idea that rather then fitting the model to the data output as in the previous case study, the output can be characterized as either a background endemic condition or an outbreak condition. In most microbial risk assessments, such as the one discussed in Section 2.1 on developing control strategies for minimizing risks associated with swimming, incidence data is lacking (Eisenberg et al. 2002, Eisenberg et al. 1996). In this manner the output is classified into one of two categories. To obtain the output needed for classification, probability distributions are assigned to each model parameter and multiple simulations are conducted. Specifically, for each simulation, a set of parameter values is obtained by randomly sampling the parameter distributions. The distributions are uniform unless the parameter range spans more than two orders of magnitude, in which case a log-uniform distribution is used to more efficiently explore the full range of values. Assigning a bounded uniform or log-uniform distribution to each parameter allowed us to take into account data from various literature sources without biasing towards one value or another. A binary classification algorithm is then applied to each simulation output, in which the output either passes or fails a set of criteria. This binary classification is essentially a goodness-of-fit criterion based on whether or not the output is representative of the data. The multivariate parameter distribution associated with a background/above background classification is then analyzed using any of a number of classification algorithms. The details of this approach are given in a previous publication (Eisenberg et al. 1996).

Modeling Outbreaks and Developing control strategies

General models for insight development

Our first aim of this objective will be to develop general models that will provide general insight. These insights will in turn help in the construction of models formulated to address specific control decisions in specific circumstances. We will perform sensitivity analyses for the final size of epidemics across the full feasible parameter space. Model exploration for sensitivities will be first performed using deterministic compartmental models with broad definitions of environmental sites. This will be followed by using stochastic compartmental models in those parameter spaces found to be of interest in the deterministic compartmental model exploration. To obtain heterogeneity at the individual level, for example to examine the impact of superspreading events, requires more detail than a compartmental model provides. For these applications, individual-level event history models will be developed.

When any surprising sensitivities are found at any level, we will proceed to explore model behavior until we have logical explanations for these. Using linked models across different model forms helps in finding insightful explanations. For example, to explain a surprising sensitivity found using the deterministic compartmental model form, individual event histories might be followed in the comparable individual event history model to check out hypotheses about why the behavior is occurring.

Scenario models for evaluating bioterrorist control strategies

Using the insight from our general model analysis, more specific and detailed models will be formulated to examine specific control decisions. For example, we will develop models for SARS to examine different contamination scenarios such as: 1) from single introductions; 2) from massive contaminations in restricted environmental sites; and 3) from diffuse introductions all at one time or over time affecting widely scattered individuals. We will borrow from our own experience analyzing the Beijing SARS epidemic as well as the work of Bozzette et al. (Bozzette et al. 2003) who examined control scenarios for smallpox threats.

One important focus in this grant will be to examine decontamination as a control measure. In the Beijing SARS epidemic, decontamination was an expensive and disruptive activity that was never well evaluated and that WHO officials tended to discount. Given superspreader dissemination of infection, there is considerable potential for environmental contamination to play key roles in disseminating infection in the transmission system. Even though decontamination may potentially prevent only 10% or fewer of infections, the transmissions it prevents at public environmental sites where many people could pick up the contamination, could potentially play key roles in preventing transmission. In a bioterrorist episode, decontamination may play a larger role than in a natural epidemic.

While the focus of our SARS work within this EPA grant is environmental contamination assessment and decontamination, realistic scenario assessment requires that we specify full ranges of other control efforts. The difference will be that we will not pursue analyses to make decisions for other control modes. We will just take them as given events and explore decisions about decontamination in the context of those given events.

Environmental contamination will also be the focus of our waterborne transmission work. A primary question for these pathogens (focusing on noroviruses as our marker pathogen) will be on the comparison between localized and centralized control. Our previous work has suggested that there are certain important tradeoffs between intervening at a local level by supplying individuals with water treatment devices or at the central level by improving water treatment at the drinking water plant. These tradeoffs depend heavily on transmission patterns. Similarly, contamination of surface waters can be addressed locally by limiting exposure or centrally through treatment processes.

We will construct environmentally mediated models as described above to account for the geographic patterns of infection that were observed. In our scenarios the public health personnel will take either a general control approach, such as mass vaccination, or a more focused approach, such as targeted vaccination. The decision whether or not to focus control efforts is one of the most important in public health. Logistically it can be demanding to focus efforts. One must have a strong rationale for doing so. Thus most major public health control efforts like mass vaccination programs are designed for general rather than focused coverage. But decontamination of environmental sites where transmission has occurred or where a bioterrorist might have seeded an agent must be focal in order to be practical. Given limited resources, the issues are how much of available resources should be dedicated to

decontamination and where should decontamination take place as well as when and where barrier protections like masks and gowns will contribute most to epidemic control. The use of masks, for example, by the general public was found to be protective against SARS infection both in Hong Kong(Lau et al. 2004) and Beijing(Pang et al. 2003).

Using our Beijing SARS models elaborated to the local level and in individual event history form with incorporated public health personnel, we will explore bioterrorist control potential given single introductions, massive focal contaminations, and multiple small contaminations at dispersed sites that occur simultaneously or over time. For each scenario we will explore 100 different parameter settings chosen consistent with the approach used in the attached paper. This will be a more complex task than that presented in the paper, however, as the model will be more detailed and will be stochastic. Again our linkages to other model forms will be essential to choosing the 100 parameter settings for further exploration.

Likewise, we will also modify these models to examine analogous water related control issues for a variety of exposure events with noroviruses. As with the SARS example, we will focus on three types of contamination: single introductions, massive focal contaminations, and multiple small contaminations at dispersed sites that occur simultaneously or over time.

Developing analysis strategies that can be used in emergency situations

We cannot expect analyses made prior to a bioterrorist emergency to guide us through control of that emergency. Too much is unknown and variable. We must depend upon fast and accurate analyses during the emergency. Our Beijing analysis clearly demonstrates that the models used for such an analysis must realistically capture key aspects of the nonlinear dynamics of infection transmission and the nonlinear dynamics of control actions like contact tracing and quarantine. It also indicates that assessment of temporal patterns for contact behavior will be helpful. But this deserves further exploration under this grant.

We will next evaluate the utility of both our airborne (using SARS as our marker pathogen) and waterborne (using norovirus as our marker pathogen) transmission models. Each model will have sufficient detail to describe environmental contamination and transport. We will use these to evaluate the utility of our model analyses approaches when many aspects of infection and environmental contamination are randomly selected and unknown to an analyst that is using computer simulation output to help make control decisions; i.e., the analyst will not know what bioterrorist scenario initiated the epidemic, what environmental sites generate the widest dissemination of cases, what environmental sites generate the greatest total number of cases, nor where aerosolization might be a problem. Given limited resources they will take data from the simulations, fit models to that data, and make decontamination decisions on the basis of that data. Their ability to decrease epidemic size in comparison to epidemics where no decontamination or unfocused decontamination takes place will be analyzed as a function of the models and data used as well as the situations generating the epidemic.

Using environmental measurements to guide control actions

Within the above analysis of simulated epidemics will be the use of varying levels of data on contamination levels at different sites and varying levels of sensitivity and specificity of such data. For SARS, these data will not be confined to the analysis of decontamination decisions. We will evaluate its use in fitting epidemic models for the purpose of evaluating the three control modes addressed in our attached submitted paper. To this end, we will use individual event history models to generate the data and deterministic compartmental models that explicitly model environmental contamination to analyze the data. We will compare the accuracy of

assessment of the three control methods addressed in our paper with and without the environmental data. For norovirus, will plan to evaluate different environmental sampling strategies, such as, comparing using low detection limit methods and lower sampling frequency in time and space, with using high detection limit methods and higher sampling frequency in time and space. We will also examine the most efficient sampling strategy given variability in environmental contamination levels.

We suspect that given environmental contamination data, a more accurate assessment of the effects tracing and quarantine, early diagnosis, and general contact reduction will be possible than without the environmental contamination data. If that is the case, then even if we show that decontamination will not contribute much to epidemic control, our models will be particularly productive. Note that environmental contaminations do not have to be viable to provide this sort of utility nor for that matter to help direct decontamination efforts. They merely have to indicate that environmental contamination has taken place. If this in fact proves useful, it should stimulate the development of more readily deployable environmental monitory technology of the needed sensitivity and specificity levels.

Expected Results and Benefits

Our work will contribute essential elements to control of a bioterrorist disease outbreak related to infections transmissible via water or combined droplet and airborne routes. It will determine the agent, host, and environmental aspects of an outbreak that make environmental sampling, environmental decontamination, and institution of barriers to environmental exposure worthwhile. It will provide general insights as to when and where environmental sampling will be most informative in guiding control decisions and when and where environmental decontamination and exposure barriers will be most productive. It will also provide general insights as to what environmental sampling strategies with regard to frequency, intensity, and spatial and social extent of sampling is indicated. Likewise it will define what other exposure surveillance activities like monitoring of public behavior over the course of an outbreak will contribute most to epidemic control decisions. Our work will determine the relative contributions of decontamination versus contact tracing and quarantine, improved diagnosis and isolation, and behavioral change that reduces exposure or contact. It will be especially helpful in determining when and where airborne exposure reduction measures like wearing masks and fomite contact measures like wearing gowns will contribute most to epidemic control, or conditions when and where household advisories on boiling or filtering water would be warranted.

Our work will also contribute essential tools for analyzing bioterrorist emergency situations involving transmissible agents. We will define what model forms and model details are needed to make robust inferences about the effects of control actions from different levels of information that might be available.

This transmission modeling activity will define what level of detail in environmental exposure models will contribute control decisions. Likewise it will define what areas of research and development of environmental sampling and analyzing methods will contribute most to the control of transmission.

General Project Information

Dr. Eisenberg will be the lead investigator at UC Berkeley and Dr. Koopman will be the lead investigator at University of Michigan. Each will be responsible for the overall research

plan during the model development and analysis phases of the project. Dr Eisenberg will focus on waterborne transmission and Dr. Koopman will focus on airborne transmission. Each institution has office space and computer access for the investigators and graduate students on the project. At UC Berkeley, Dr Alan Hubbard will assist in the development of statistical techniques for the analysis phase of the project and Dr. Reingold will provide expert advise in developing the outbreak scenarios and providing interpretation to results. Dr Hubbard is a recognized expert in statistical applications to epidemiology. He is has developed statistical techniques for risk assessment and has co-authored a number of publications with Dr. Eisenberg. Dr. Reingold is a recognized expert in infectious disease epidemiology with particular experience in surveillance activities and outbreak investigation. Even before 9/11 he was a recognized expert on the public health issues associated with bioterrorism. He is currently the Principal Investigator for the Center for Infectious Disease Preparedness (funded by the CDC), a training center to prepare state and local health officials for bioterrorist incidence.

The following is a work schedule for the duration of the five years.

	Year 1	Year 2	Year 3	Year 4	Year 5
2.1 Model Development					
General transmission models					
Environmental models					
Integration transmission and environmental models					
2.2 Model parameterization and Identifiability					
Database development					
Refining statistical techniques					
2.3 Modeling outbreaks and developing control strategies					
Insight development					
Scenario development					
Model analysis: emergency situations					
Model analysis: defining environmental sampling strategies					

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Project III. Dose Response Assessment

Objectives

In the risk assessment framework there are a number of sources of heterogeneity. Some sources are clearly associated with heterogeneity in exposure. However others are functions of heterogeneity amongst the individuals or within the population that is exposed.

The sources of heterogeneity in the effects assessment include the following:

Variability in the intrinsic infectivity and virulence of the infectious agents (including potential alterations from "weaponization" of organisms of concern)
Variability in the response of individuals to the infectious agent (and modification by intrinsic and extrinsic factors influencing susceptibility)
Immune status (outcome from prior exposure and alterations due to other physiological factors)
Differences in exposure to infected individuals in the contagious state (presence of "super-spreaders" or failures of quarantine or containment)
Behavioral and venue differences affecting the exposure to sources of contagion arising from a primary infected individual
Differences in severity and duration of outcomes resulting from exposure

The first three factors relate particularly to the dose-response relationship (although the duration and strength of initial immunity relates also to the prior transmission dynamic in an exposed population). The remaining factors relate primarily to population transmission modeling.

It is generally envisioned that bioterrorist attacks will occur through the environment. The record of bioterrorist incidents and biocrimes (Carus, 2001), as well of "natural" infectious disease outbreaks illustrates the myriad potential routes of exposure. Risk assessment models, therefore, must have an explicit description of the exposure pathways that are relevant for bio-terrorist activities.

Regardless of the route of exposure, knowledge of the dose-response relationship is needed to conduct either a static (individually based) or dynamic (population risk assessment considering disease transmission pathways) risk assessment. The objective of this project is to comprehensively review and analyze dose response relationships for potential bioterrorist agents. This will facilitate quick decision making (in the context of an emergency response), and comprehensive risk-based assessment of cleanup alternatives.

Approach

Development of Dose-Response Relationships

We will develop critically reviewed dose-response relationships for the bioterrorist agents of greatest concern that could be transmitted via inhalation in the workplace. These could be used to develop PEL's, acceptable clearance criteria, and for other regulatory and action level purposes. The work we will conduct includes the following activities:

We will perform a thorough literature review to obtain data (on CDC category A agents) that could be used to develop dose-response relationships for the agents of concern. This will include information obtained from animal and human studies. We will outreach to potential governmental and other sources of unpublished data to incorporate into our analysis.

We will critically evaluate these data for applicability.

We will test mathematical formulations that have been used in other quantitative microbial risk assessment applications and compare their performance to empirical relationships, e.g. log-probit, that have been used in other applications. Mathematical formulations will include dependence on additional variables (e.g., particle diameter, gender, age) as the data warrants.

We will review the literature for human outbreaks of illness resulting from inhalation exposure to these agents – of particular interest are studies that contain information on both morbidity/mortality rates and exposure.

We will compare the experienced morbidity/mortality rates found in outbreak studies to the predicted morbidity/mortality rates estimated (using the exposures that resulted in the outbreak) from the dose-response relationships developed so as to validate the use of those dose-response relationships for assessing human risks.

We will develop and test a next-generation of dose response models considering details of *in vivo* transport and fate of pathogen to the site of colonization and infection

We will conduct animal experiments to extend the knowledge base found in the prior literature, particularly with respect to quantifying physiological parameters that can be used in more sophisticated dose-response models, and elucidating the impacts on susceptible subpopulations.

The concept that exposure to infectious organisms can be described by a dose-response relationship has been explicitly acknowledged since at least the 1950's (Wells, 1955). This concept was elaborated upon by Riley and O'Grady, who recognized that there may be various intrinsic and extrinsic modifiers to infectivity of organisms (Riley and O'Grady, 1961).

Since the early 1980's (Haas, 1983; Haas *et al.*, 1999) a paradigm for describing risk from exposure to microorganisms has emerged in which the standard risk assessment techniques are employed to estimate risk from pathogenic microorganisms. A number of senior personnel on the CAMRA team have been integral to the development and advancement of this paradigm. These techniques primarily have been applied to various ingestion (Regli *et al.*, 1991; Crockett *et al.*, 1996; Haas *et al.*, 1996; Medema *et al.*, 1996; Cassin *et al.*, 1998; Gale *et al.*, 1998; Teunis *et al.*, 1999) and dermal exposures (Rose and Haas, 1999).

Only more recently has quantitative microbial risk assessment (QMRA) been applied to inhalation exposures, in the context of bioaerosol emissions from sludge disposal operations(Dowd *et al.*, 2000). The PI of this project has developed the first (known) dose response relationships for the inhalation of *Bacillus anthracis* spores (Haas, 2002).

Searching for Data

The data needed to perform dose-response analyses, and to validate the models against human outbreak/accident reports will be obtained from a comprehensive literature review. The process for reviewing the literature can be divided into two phases -- bibliography development and assessment/extraction of information.

To develop a bibliography we shall rely to a large degree on computer-based search strategies. Our primary databases of use are anticipated to be *Index Medicus* (available publicly

at http://www.nlm.nih.gov) and *Web of Science* (the electronic version of *Science Citation Index*), which is available at Drexel University. We plan to use both subject-based search strategies and citation based search strategies to extend our bibliography to the maximum extent possible. We will also be aided by our collaborators on the knowledge discovery effort in CAMRA with respect to devising and perfecting our information search methods.

Subject based search strategies will focus on running various keyword combinations to acquire citations that (based on title and abstract) appear promising. We will in general combine terms describing organism and disease (e.g., *Francisella tularensis* or tularemia) with terms denoting outcome, exposure route or endpoint. An initial glossary of terms is shown below. In formulating our descriptors for organisms we will use both old and superseded taxonomic nomenclature.

Organism/Disease Terms		Outcome/exposure/endpoint terms
Variola virus Variola major Variola minor smallpox *Bacillus anthracis* anthrax *Yersinia pestis* *Pasteurella pestis* (*) Pneumonic plague	*Francisella tularensis* *Pasteurella tularensis* (*) *Bacterium tularense* (*) tularemia Filovirus Arenavirus Ebola virus Lassa virus	Inhalation Infectivity Outbreak Dose-response Aerosol

(*) Superseded taxon

As an example of subject-based strategies, use of the terms **Filovirus** and **infectivity** in *Index Medicus* results in a number of hits, including one in which cynomolgus monkeys were exposed to the Ebola-Reston strain of virus by aerosol (Jahrling *et al.*, 1996). Based on the title and abstract, this reference appears to possibly contain useful data, and would be acquired.

As an example of citation-based strategies an *Index Medicus* search on the combination of ***Yersinia pestis*** and **infectivity** yields a reference on efficacy of antibiotics in treatment of pneumonic plague in mice (Byrne *et al.*, 1998). Examination of the bibliography of that paper yields a 1948 case report of an outbreak of pneumonic plague (Tieh *et al.*, 1948). Use of the citation search capability in *Web of Science* shows that there have been 10 citations to the 1948 incident report including a letter appearing in 1994 on plague infectivity (Cowling and Moss, 1994). In this manner a network or web of references can be developed to form the starting point of the analysis phase.

There is interaction between the subject matter search approach and the citation search approach. As illustrated in **Figure 1**, references located via a subject matter search can be used as starting points to "search forward" in a citation search. The former can also be used (via selection of references in the literature cited therein) to locate earlier sources which can be used as additional entry points into a citation search.

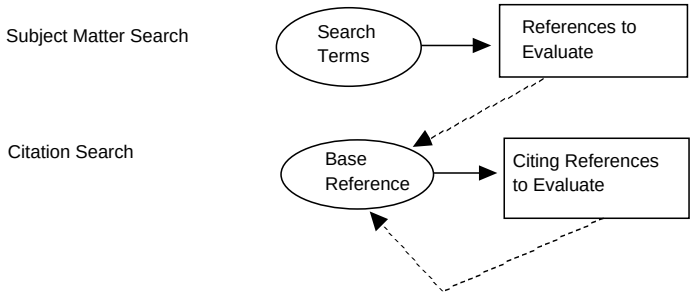


Figure 1 Search Strategies.

Additional sources to be examined (both for information and for citations to the primary literature) will be monographs and review articles. The USAMRIID handbook on medical management of casualties forms one significant such monograph (U.S. Army Medical Research Institute Of Infectious Diseases, 2001). The reviews of specific agents, for example on plague (Inglesby *et al.*, 2000) are examples of major review articles serving as starting points for a search strategy. CDC and WHO web sites will also be searched for applicable monographs and reports. We will also do a web search, using standard search engines (e.g., Google) to obtain leads on additional data sets (reports, for example) that are not covered by the journal data bases.

To the degree which information may be available in gray sources, we will use our contacts to obtain this. For example, Professor Haas has been on several committees of the National Academy relating to bioterrorism, and he also has served on a working group on dose response modeling convened by the US Army Center for Health Promotion and Preventive Medicine (CHPPM) and has thereby become familiar with (some) agencies that may have data. However for security classification reasons, such data may or may not be accessible.

Data Acceptance Criteria

Once a bibliography is established, it is necessary to examine each of the references and ascertain whether or not useful data can be extracted. For this purpose, it is necessary and desirable to define data acceptance criteria. The details of the criteria differ for information to be used for developing dose-response relationships, and for information used for validation (from outbreaks or human case reports). The acceptance criteria for the two classes of information are detailed below.

Dose-Response Information

To be useful as a source of dose-response data, the study must report the number of subjects (e.g., animals) that are administered particular doses of microorganisms and the mode of administration. Of those exposed, the number that have been regarded as positive (infected, ill, dead) must also be recorded. The criteria for positive endpoints, such as definition of infection, must be detailed. The mode of preparation of the inhaled organisms must be described including characterization of the particle diameter, since the infectivity of aerosols is dependent on particle size (Watson and Keir, 1994). The organisms must be measured by an appropriate assay specific for the organism in question. Data sets that meet these quality screens will be used for analysis.

Outbreak Data

To be useful for validation of dose response relationships, outbreak (or case) reports must contain the following information:

Number of subjects exposed
Number of subjects affected
Estimation of exposure (distribution). In the absence of this, sufficient information about the mass released and dispersion characteristics to allow estimation of the exposure distribution, for example using the approach taken by Meselson *et al.* in regard to the Sverdlovsk accident (Meselson *et al.*, 1994; Meselson, 1995).
Duration of exposure
Endpoint examined (infection, illness, mortality).
Differentiation between primary and secondary cases.
Characteristics (size) of inhaled particles.

It is likely that outbreak information will frequently (as in the case of the Sverdlovsk incident) not contain all of the above information. In these cases, the missing information will be estimated based on best available resources – for example population maps, meteorological records, etc.

Candidate Models

One intrinsic feature of risk assessment is that the data used to define a dose-response relationship are most often of necessity obtained at relatively high dose (and risk) levels Hence a mathematical relationship is necessary to extrapolate to depict the risk at lower exposure levels. This problem occurs both with chemicals and with microbial agents. It has long been known, for example see (Van Ryzin, 1980), that different functional forms of dose response relationships may yield quite different low dose risk levels. Hence the use of a particular mathematical relationship must be constrained by a belief that it provides a plausible representation of the underlying process[1].

For over fifty years, it has been known that the single organism hypothesis[2] produces results consistent with observed infection dose response. Some early historical work on this point are the studies of Lauffer and Price on virus (1945), Goldberg *et al.* (1954) on respiratory bacterial and viral agents, and Meynell and Stocker (1957) on *Salmonella.* This is also supported by recent work on occupational inhalation of *Mycobacterium tuberculosis* (Nicas, 1996).

From a basic point of view, an individual viable organism contains all of the information necessary to reproduce. Perhaps the most persuasive lines of evidence for the single organism hypothesis, other than pure fits to dose response curves, have been reviewed by Rubin (1987).

The two most successful models consistent with the single organism hypothesis have been the exponential and the beta-Poisson models(Haas *et al.*, 1999); both of which (**Table 1**)

[1] The word "belief" is used deliberately, since it fundamentally impossible to prove the truth of a particular relationship, rather than to fail to disprove its applicability.
[2] That a single organism is sufficient, if it survives the defense mechanisms, to initiate the infection and disease processes.

share the characteristic that the risk at low doses is a linear function of dose. It should also be noted that the consistency between outbreak data and risks extrapolated from human volunteer trials has been demonstrated in a number of situations, for example (Rose *et al.*, 1991; Haas and Rose, 1994; Crockett *et al.*, 1996). It should also be noted that the exponential, as well as a mixture of the exponential distribution that is equivalent to the beta-Poisson has been employed in assessing risks from the inhalation of *Mycobacterium tuberculosis* (Nicas, 1996).

Table 2 Schematic Layout of Dose-Response Assay.

set	Average dose of microorganisms	number of subjects in the set	positive subjects (*)
1	d_1	n_1	p_1
2	d_2	n_2	p_2
3	d_3	n_3	p_3
4	d_4	n_4	p_4

(*) with infection, illness, death, or some other positive indicator of response

Table 1. Exponential and Beta-Poisson Dose Response Models.

Model	Equation (risk=)	Reference
Exponential	$1-\exp(-kd)$	(Wells, 1955; Haas *et al.*, 1999)
Beta-Poisson	$1-\left[1+\frac{d}{N_{50}}\left(2^{1/\alpha}-1\right)\right]^{-\alpha}$	(Furumoto and Mickey, 1967; Haas, 1983)

The Beta-Poisson equation is a simplified form of a model which can be written in terms of the confluent hypergeometric function (Furumoto and Mickey, 1967; Haas, 1983; Teunis and Havelaar, 2000).

The data obtained will be fit to the exponential and beta Poisson models. In addition, the use of models in which more than one colonization is needed to cause the effect will be tested (Haas *et al.*, 1999). The suite of empirical models employed by Holcomb *et al.* (1999) will also be explored.

Fitting Criteria

Given a set of data on infectivity, or some other endpoint (such as illness, or even mortality), we would like to obtain the best fit to a particular dose-response model. In general, the data set available for dose-response analysis is one in which several sets of subjects (either human or animal) are each exposed to a known mean dose, and the subsequent response, in terms of infection, illness, or mortality, is determined. Nomenclature for dose-response studies is given in **Table 2**.

A particular dose-response model is selected for study. This model is characterized by a function, which predicts the proportion of positive responders given dose and values of one or several dose response parameters. In a generic sense, we can write the predicted response as $\pi_i = \mathrm{P_I}(\mathrm{d_i};\Theta_i)$, where Θ is the set of dose-response parameters. We will also define the response for each set based strictly on the observations as $\pi_i^0 = \frac{\mathrm{p_i}}{\mathrm{n_i}}$. If the individual subjects have independent responses, then the overall system can be characterized using a similar likelihood framework as was used for analyzing dilution assays. This unconstrained

optimization problem can be solved numerically as we have previously utilized (Haas *et al.*, 1993; Haas *et al.*, 1996; Haas *et al.*, 1999). This problem can be solved in EXCEL (Haas, 1994), MATLAB or Mathematica. Goodness of fit can be ascertained using a likelihood ratio test on the residual deviance from the best fit (Morgan, 1992).

If we have two dose-response models, where model 2 is a special case of model 1, with numbers of parameters m_1 and m_2, where $m_2<m_1$, then we can compare the statistical significance of the improvement in fit by examining against a $\chi 2$ distribution with $m_1–m_2$ degrees of freedom. The null hypothesis (that the fits are indistinguishable) is rejected if the difference in deviances exceeds the critical value, i.e., if the difference is in excess of the critical value, then we are justified in accepting the more complex model (with more parameters) in comparison to the more parsimonious model.

Incorporation of Explanatory Variables

If data sets are found in which there is evidence for the possible dependence of response on an explanatory variable (e.g., age, gender, confounding exposures), then it is possible to test this possibility and to account for this in a dose-response modeling framework. As an example, suppose that the illness as a function of dose is assumed to follow an exponential relationship but that it is further assumed that there is a lifelong buildup of immunity that follows a separate exponential relationship as noted below:

$$k = k_0 \exp\left(-\frac{\text{age}}{\tau}\right) \qquad \textbf{(1)}$$

where τ is a time constant for the buildup of immunity, and k is the dose-response parameter (**Table 1**). The combined model, consisting of the exponential dose-response relationship and **(1)** can be estimated via maximum likelihood to determine the parameters k_0 and τ. The significance of the putative explanatory variable can be determined by likelihood ratio comparisons.

Error Bound Estimates and Comparisons of Data

An extension of the method of bootstrapping residuals appears to be suitable for dose-response data (Efron and Tibshirani, 1993). In prior work (Haas *et al.*, 1993), we have used this approach in assessing risk from ingestion of viruses from drinking water.

If we have several data sets, perhaps taken by different investigators, or on different microorganisms, or in different hosts (human and animal, or two animal data sets), a logical question to ask is whether the results of the two data sets can be pooled. In other words, can we characterize both data sets by the same dose-response relationship? This may be tested by also using a likelihood framework as in our work on *Shigella* (Crockett *et al.*, 1996). The inability to pool data may point to important mechanistic features. These may include differences in species sensitivity, or the possession of virulence factors(Ewald, 1991; Levin, 1996; Haraldo and Edberg, 1997).

Another approach to modeling strain heterogeneity is to regard individual strains as having been randomly sampled from a population of strains that could be used, and to estimate the hyperparameters associated with the between strain distribution of dose response parameters (which may be bi or multivariate). This approach was used by Teunis *et al*.(2002) in interpreting

the infectivity of multiple strains of *Cryptosporidium* and if the data suggest it, it is one that we will test.

There are some particular considerations that are appropriate to developing dose-response relationships for bioterrorist agents that will merit special consideration. These include:

For inhalation agents, it is known that the size of the aerosol in which the infectious agent is contained influence pathogenicity (Druett *et al.*, 1953), and therefore consideration of this as an explanatory variable may be necessary (or this may explain differences between data sets)

"weaponization" or other surface treatment may influence retention and ultimately infectivity of an agent. While it is not likely that we will be able to obtain data from the open literature on this, it may be that sufficient data is available for a particular organism prepared under different conditions to inform dose response modeling.

There may be changes in infectivity and virulence that can be correlated to genetic features – or alterations. The concept of virulence-factor-activity relationships (VFAR's), which will be studied in the one of the other CAMRA projects will be used to inform our incorporation of these changes in dose-response modeling.

Validation

We anticipate that most or all of the data sets used for construction of dose-response relationships will be based on animal studies. Validation against human data from outbreaks or accidents becomes important in assessing whether the animal-derived dose-response relationships provide an adequate descriptor of human risk. This will be a fundamental hypothesis that this study is designed to test. This will enable us to ascertain whether it may be necessary to correct for differences in lung deposition (especially in the alveolar region) of fine particles between species, as suggested in the context of non-biological particle deposition investigations (Palm *et al.*, 1956; Kliment *et al.*, 1972; Miller, 2000).

The test of validation will be whether the risk predicted from use of the dose-response relationship(s) used with the exposure conditions for particular outbreaks are in concordance with the observed attack rates during those outbreaks. We will consider the formal uncertainty estimates obtained from bootstrapping dose-response curves, and in exposure estimates, along with uncertainties in estimation of attack rate (for example sampling errors) in undertaking this comparison. Our work with the oral exposure to *Escherichia coli* O157:H7 illustrates (Haas *et al.*, 2000) the validation process.

Development of Physiologically Based Dose-Response Models (PBDRM)

The microbial dose-response curves discussed above share a common feature in that they describe the end-point effect as a function of the administered dose (i.e., number of organisms ingested or inhaled). However the actual dose that is important in the causation of infection/illness is the dose delivered to a location where colonization can occur (and ultimately the number of organisms *in vivo* subsequent to colonization). This process can be described graphically (in the case of *Bacillus anthracis*) as in **Figure 2**. We hypothesize that if we can effectively predict the delivered dose (e.g. number of organisms inhaled and retained in the alveoli in the case of *B.. anthracis*) or the body burdern (number of organisms that have multiplied *in vivo* at the colonization site), we can more precisely predict the risk than only by using administered dose. This is a parallel to the use of PBPK models in chemical risk assessment (Chinery and Gleason, 1993; McKone, 1993; Committee On Risk Assessment Of Hazardous Air Pollutants -- Commission on Life Sciences, 1994).

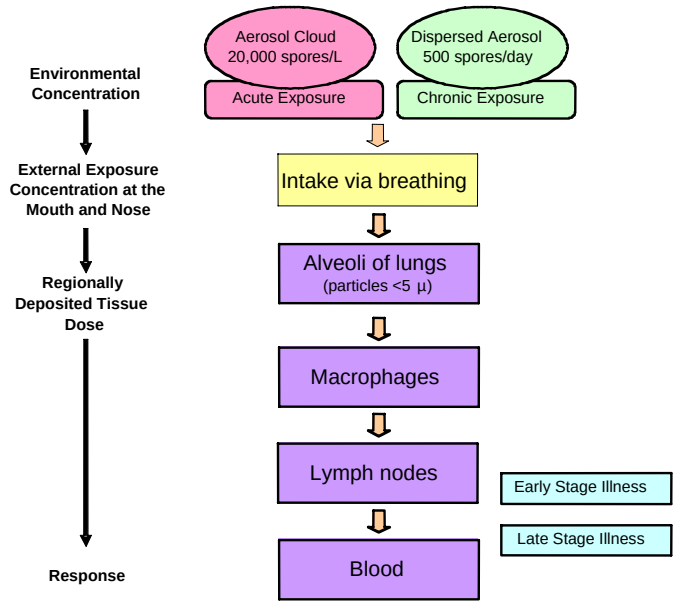


Figure 2. Conceptual Diagram of *in vivo* fate of *Bacillus anthracis*. From Thran et al. (Personal Communication)

To employ this approach it is necessary to describe the processes governing the fate and transport of infectious agents from the portal of entry to the site of colonization. During the latter half of the project period, the literature will be reviewed for knowledge of such processes, and particularly their quantitative modeling, and physiologically based dose-response models (PBDRM) will be developed in which the end effect is modeled as a function of the delivered dose. We will benefit from the knowledge of Dr,'s Nazaroff, Nicas and McKone, who have worked on the modeling of inhalation transfer of pollutants with respect to inhaled agents.

We hypothesize that the use of this approach, if demonstrated to be useful (which we will test by fitting dose-response data using these formulations) would offer the following benefits:

It may offer the ability to predict the impact of different physical formulations on agent potency. For example, could the correction from administered dose to delivered dose quantitatively predict the effect of particle size on infectivity observed by Druett (1953) in the case of *B. anthracis* inhalation

It may offer the ability to extrapolate between species if the primary difference between species is the delivery of the agent to the active site (or if the differences in intrinsic *in vivo* immune response could be quantitatively described for the various species of interest).

The animal experiments discussed in the next subsection will help inform the development of PBDRM's.

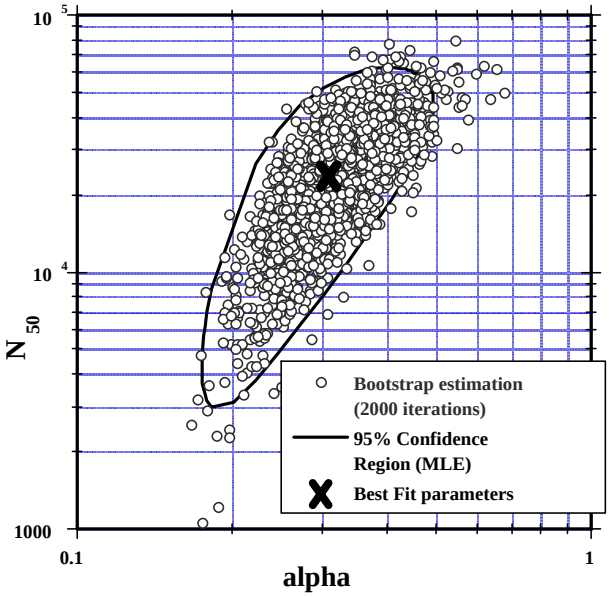


Figure 3. Bootstrap and Likelihood Confidence Regions for Dose Response Parameters from *Salmonella* Ingestion. (From (Haas *et al.*, 1999))

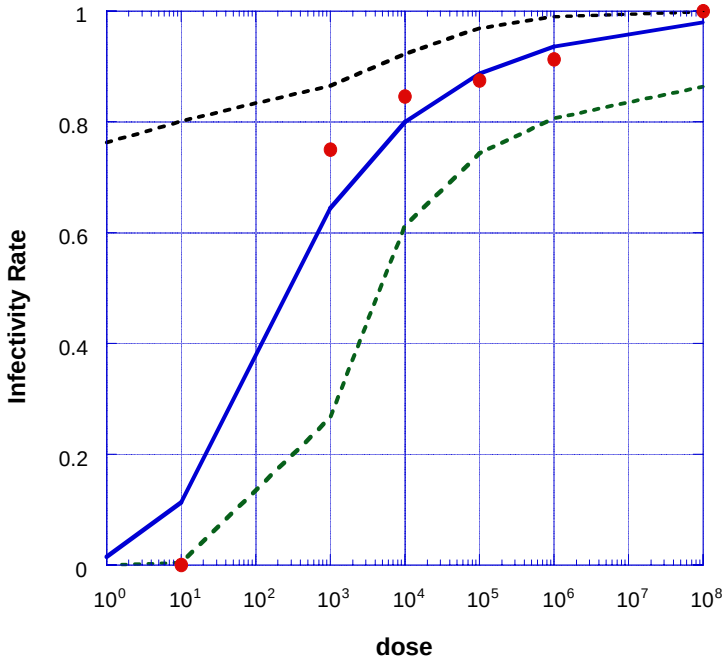


Figure 4. Best Fit Beta Poisson Dose Response for Ingestion of *Vibrio cholerae* with upper and lower 95% likelihood based confidence limits. From (Haas *et al.*, 1999).

Animal Dose-Response Experiments

The approaches outlined here for mining existing data to estimate key dose-response parameters are likely to identify significant gaps in dose-response for one or more pathogens. To determine if highly target experimental data will serve to fill these gaps and provide a better foundation of the risk assessment model, we propose to conduct a series of experiments to define the dose-response relationship between two List A pathogens in relevant model hosts. In addition, because a bioterrorist event will likely result in significant contamination of the environment including surfaces, soil, and water, we will determine the dose-response relationships for exposures that occur by ingestion and topical exposure. In addition, we will examine changes in the dose response that occurs in particularly susceptible populations.

The animal experiments will be carefully planned to provide precise data to inform the risk assessment models. Numbers of animals required to develop useful dose response parameters will be determined in concert with Dr. Haas and others on the CAMRA team. We will conduct experiments with 2 pathogens (*Francisella tularensis* and *Yersinia pestis*) in relevant animal models. We have chosen these pathogens to study because they are both of significant concern as potential bioterrorist agents, they have very wide host ranges and therefore can persist in the environment or reservoir hosts following an event, and there is incomplete information in the literature regarding dose-response parameters.

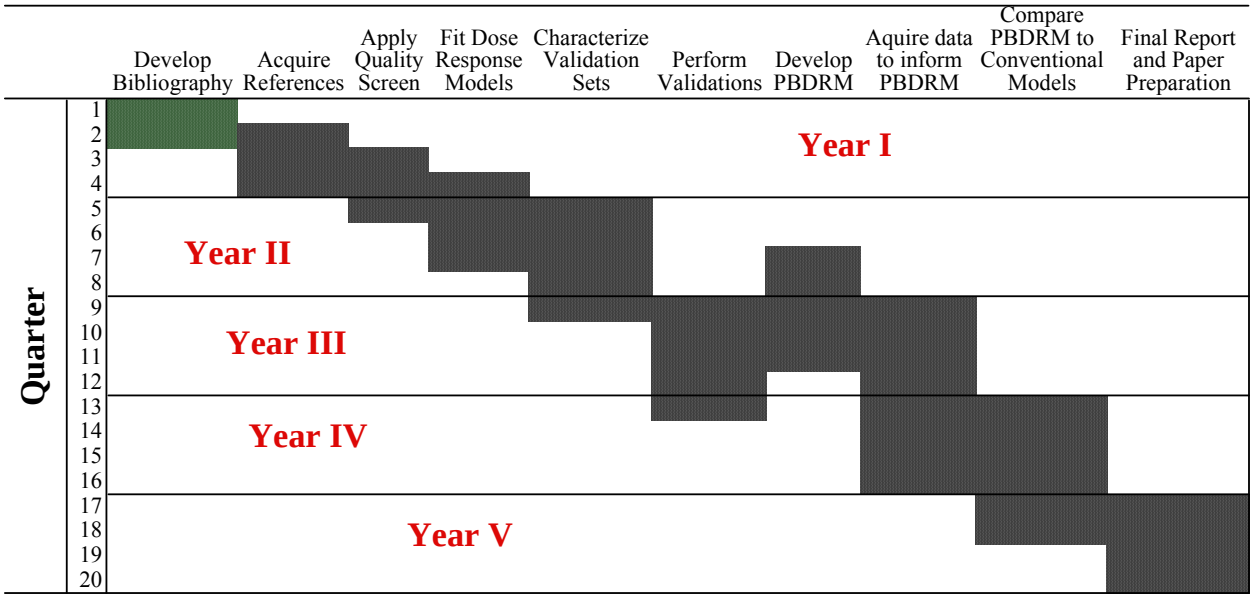
Francisella tularensis subsp *tularensis* causes tularemia and is a small Gram-negative facultative intracellular pathogen that has a very large natural host range with over 100 species of wild animals, birds, and arthropod vectors being involved. Most human infections are associated with contact with rabbits, and rodents or their habitats and these species are important in maintaining the infection in enzootic areas (Ellis *et al.*, 2002). Biting insects may also play a role as mechanical vectors for Francisellae. Francisellae are also known to infect and persist in aquatic protozoans and water-associated outbreaks have been documented (Anda *et al.*, 2001; Tarnvik *et al.*, 2004). The typical primary routes of exposure for humans under natural conditions are associated with outdoor activities via contact with contaminated air, water, soil, or vegetation or by handling ill or dead animals. Clinical signs of tularemia in humans and animals depend on the route of exposure, the virulence of the infecting strain, and the immune status of the host (Ellis *et al.*, 2002). In concert with the CAMRA team we will examine the available literature on the dose-response of *Francisella* in animals and humans and identify parameters which need to be determined or validated experimentally. Mice are a good animal model for *Francisella* although there is some variation in the susceptibility of various mouse strains (Shen *et al.*, 2004; Chen *et al.*, 2004). Most infection and vaccine studies have used intradermal inoculation as the route of exposure and more recently aerosol challenge models have been standardized (Shen *et al.*, 2004; Chen *et al.*, 2003). These experiments have identified median lethal doses for *F. tularensis* type A and B. There is comparatively little information regarding the dose-response following contact exposure or ingestion (Stenmark and Sjostedt, 2004; Meinkoth *et al.*, 2004).

Yersina pestis causes the Plague and is a Gram-negative rod which is closely related to a number of intestinal pathogens and has a wide mammalian host range. Rodents are the natural reservoir of *Y. pestis* and the infection may be transmitted by biting insects, aerosol, contact, or ingestion (Perry and Fetherston, 1997). As in tularemia, the clinical signs and clinical outcome differ in human and animal *Y. pestis* infections based on the route of exposure. Experimental studies have been done with subcutaneous inoculation of mice with *Y. pestis* and with a flea-bite

infection model (Russell *et al.*, 1995; Garmory *et al.*, 2004; Mencher *et al.*, 2004; Jarrett *et al.*, 2004). In each of these situations the infection progresses quickly and is highly lethal. There is little information about the dose-response relationship with other routes of exposure.

We propose to study the dose-response relationship between *F. tularensis* and *Y. pestis* in BALB/C mice that are exposed by aerosol, intradermal inoculation (to mimic insect bites), ingestion, and contact routes of exposure. In the first experiments, dose-response parameters will be described. In subsequent studies, detailed histopathologic and culture studies will be performed to determine sites of initial colonization and subsequent spread to other tissues. Other studies will examine differences in dose response in special populations including weanling and geriatric mice. These data will be used to validate data mined from the literature and to provide a firm foundation for risk assessment of the consequences of an intentional release of this agent.

Figure 5. Anticipated Project Timeline for Modeling and Literature Review.



Expected Results and Benefits

This project will produce a reference set of critically reviewed dose-response relationships for Category A agents (in human and animal species where data are available). These will include best fit values and confidence distributions for parameters such as in **Figure 3**, and dose-response curves with upper and lower confidence limits such as in **Figure 4**.

By compiling dose-response relationships in various hosts and for various strains, in conjunction with information from other projects in CAMRA, we will be able to ascertain the inter-(microbe)species heterogeneity in infectivity, and determine whether there are discernable genetic markers which may be correlated to such differences. This may facilitate an assessment of the potential for further alterations in a strain to change potency.

General Project Information

Timeline and Personnel

Professor Charles N. Haas of Drexel University will serve as the overall manager and PI of this project. He has been doing microbial dose response and risk assessment for over 20 years. The anticipated project timeline for the modeling portions of this project are shown in **Figure 5**. He will be supported by graduate research assistants (1.5 in years 1, IV and V; 2.5 in other years) and by a part time undergraduate in year V.

Professor Carole Bolin at MSU will be in charge of all animal experimentation. She will be supported by a graduate student for the duration of the project and has available experienced technical support that are trained and registered for work with Select Agents. Studies will be planned in Year 1, conducted in Years 2, 3, and 4, and in year 5, one mouse experiment is budgeted to fill any remaining gaps and incorporation of experimental data into risk assessments will be finalized. All animal experiments will be informed by the literature reviews to be conducted, and Professors Haas and Bolin will collaborate on statistical aspects of experimental design and analysis of data.

Facilities

This project will be conducted at Drexel University in the Department of Civil, Architectural and Environmental Engineering. The environmental engineering program at Drexel has 6 faculty participating in its activities, 40 graduate students, and 30 undergraduates. Our computational facilities which will be used for this project include a cluster devoted to Prof. Haas' students, containing 5 Macintosh systems and 2 Windows systems. Drexel has a site license to SPSS, as well as routine software, and Professor Haas has maintained licenses for bibliographic and computational software (Matlab, Mathematica) for his student group. Office space is available for graduate students conducting research.

Of particular note to this project is that Drexel has received recognition as one of the "most wired" and "most wireless" campuses, and our library resources (including access to bibliographic databases such as Web of Science and Compendex) are accessible in any of our offices (including student offices) via both Ethernet and wireless connections.

Dr. Bolin is the supervisor of the Select Agent Laboratory at MSU (650 sq. ft) and of a BSL3-Ag level containment laboratory (1400 sq ft) that are part of the newly constructed Diagnostic Center for Population & Animal Health. Dr. Bolin, her staff, and her laboratories are registered for work with 9 Select Agents, including the agents identified here. All work with the highly infectious pathogens *F. tularensis* and *Y. pestis* will be conducted in BL3 containment in Dr. Bolin's labs or in BL3 containment animal facilities at MSU. Dr. Bolin also has a 4000 sq. ft BL2 laboratory and support space (biohazardous waste disposal, media preparation, etc) available to support aspects of this project.

Project management and communication

This project will be integrated into the overall structure of CAMRA by a variety of mechanisms. First, Professor Haas will serve as co-center director, and will be a member of the center steering committee. Second, he will contribute to (and benefit from) the knowledge repository which will serve as a rapid means of information exchange and discussion amongst all

center researchers. Third, he has had a long record of working with many of the other CAMRA investigators (so that time does not need to be spent in creating interpersonal ties):

He, Joan Rose and Charles Gerba have collaborated on joint research in the microbial risk assessment area, and other areas since the late 1980's.

He has worked with Dr. Eisenberg and Koopman on a number of EPA panels and other activities developing and applying risk methodologies

Professors Haas and Bolin will be in frequent contact via voice and electronic means with respect to the design, conduct, analysis and interpretation of animal studies.

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Project IV. Assessment-Analysis Interface
Lead: Dr. Patrick Gurian

The Assessment-Analysis Interface

1.0 Objectives

Estimating the risk presented by bioterrorism incidents presents a formidable challenge. Risk assessments rely on a series of interconnected models of release, transport, attenuation, exposure, dose-response, health effects, and secondary transmission of infectious agents. At the current time there are substantial uncertainties as to both the appropriate model form and/or parameter estimates for most of these models. In addition, exposure and risk are strongly influenced by the behavior of the public, and there are substantial uncertainties as to how the public will respond in the aftermath of an attack. Addressing all these uncertainties simultaneously is not feasible even within the context of a major coordinated research effort such as the one proposed here. Therefore, it is crucial that research be focused on those areas where it is likely to produce the most valuable results. This research project will use analytical approaches from statistics, decision analysis, and psychology to produce such a prioritization of research needs and to identify, and begin to address, social factors that can significantly influence risk. By focusing research efforts on productive lines of inquiry, this project has the potential to greatly improve the practical usefulness of the results derived from the proposed research center.

This project will link the technical research on bio-threats, which falls in the domain of risk *assessment* with the societal goal of managing risk which (along with risk assessment) constitutes the more general domain of risk *analysis*. This terminology was established by the National Research Council's "Red Book" (NRC 1983) in an effort to separate more objective, scientific issues from matters of public policy which are likely to be the subject of contentious debate. While this separation may be helpful in some circumstances, some linkage between technical research and societal response is necessary to ensure that the technical research is to be directed towards answering questions relevant to risk management decisions, and that the societal response plan is informed by accurate technical information.

The project will begin with an effort to identify exposure scenarios of concern (Objective 1). It will then identify the social factors that significantly influence risk management options for these scenarios (Objective 2) and the available technical understanding (Objective 3). Finally, it will integrate both technical and social factors (Objectives 4 and 5) to evaluate the effectiveness of current response options and to prioritize future research needs. A description of the approach to be followed for the realization of each of these five objectives is provided in detail below.

2. Approach

Objective 1. Identification of Scenarios and Modeling Tools

This task will develop the quantitative framework for the project by identifying a set of exposure scenarios of concern to risk managers and a set of models that can address these scenarios. Risk managers will be consulted as to the scenarios of most concern to them, the policy options they expect to have, and any existing response plans. As many of these risk managers are also

technical experts, this consultation will be integrated with the elicitation of the "expert model" (described in Objective 2 below).

There is an incredible diversity of potential bioterrorism incidents. Given that is it not feasible to study all potential exposure scenarios, the research will focus initially on a limited number of scenarios that capture the range of variation of possible incidents. At least one scenario is expected to consider the contamination of a single building with anthrax or another persistent agent. At least one other scenario will consider an outdoor release of smallpox or a similar infectious agent likely to generate secondary cases. A third will consider an attack with plague or another zoonotic disease. These types of incidents capture a range of threats from localized, long-term contamination to large-scale events requiring a swift response. The goal will be to identify a set of concrete scenarios that are amenable to quantitative risk analysis and exemplify the range of concerns confronting risk managers.

The technical literature will be reviewed to identify modeling tools and approaches to address the scenarios of concern to risk managers. It is expected that a suite of interconnected models will be identified that describe the different phenomena associated with a bioterrorism incident including release, dispersion, exposure, health effects, and secondary transmission. While basic methodological questions still exist within the field, quantitative risk analyses are beginning to be feasible often using a set of modeling tools borrowed from other domains such as food and water microbiology (see Haas 2002, or Casman, Fischhoff et al. 2000, for example). At least initially, preference will be given to simple models (with analytical solutions if possible) as these are less computationally intensive and suitable for the general, non-site-specific modeling envisioned here. The selection of models will be coordinated through meetings of the steering committee with the intent being to use the same models in this project as the other CAMRA projects. The selection of fate and transport models will be coordinated with Project I, secondary transmission models with Project II, and dose-response models with Project III. The objective will be to develop a single C-language computer program that can execute all of the selected models and pass information among them. When appropriate, reduced-form versions of the models employed by the other projects will be used in this project to reduce the computational burden.

The suite of models will be used to integrate risks from the various domains in a dynamic, behaviorally realistic, inclusive framework, and will serve as the backbone of the integrated risk assessment. This model will enable the evaluation of a variety of risks associated with attack/mitigation combinations.

Objective 2. Public Perception of Bio-threat Risks

The goal of this task is to understand how public perception of risk affects exposure and mitigative response behaviors by the public, and to identify key misunderstandings that could be corrected with targeted risk communications. The public response to a bioterrorism incident will influence the effectiveness of a wide range of supposedly "technical" risk management decisions that rely on large-scale changes to the public's behavior (e.g., evacuation, quarantine, mass-vaccination programs). For such measures to succeed, the public will need to be viewed not as bystanders who may hinder a response but as partners in responding to an incident (Glass and Schoch-Spana 2002).

In crisis situations, many experts' first impulse is to tell citizens to go away while they figure things out. It is tempting, at some times, to magnify risks in order to motivate citizens. It is tempting, at other times, to trivialize their worries, with comparisons like "why get so exercised about terror, when you're still smoking" or "only five people have died from anthrax [so far], compared with 40,000 annually from motor vehicle accidents." The rhetorical tone of such comparisons puts many people off, especially when the options differ in other ways (e.g., benefits, costs, availability of alternatives).

An academically discredited but still operational misconception is that people panic in times of crisis, behaving irrationally at the individual and group level. This is often the unstated rationale for withholding bad news from the public. People may act on the basis of poor information, to their own detriment, but the problem is with their information, not with their rational processes (Glass 2001; Fischhoff, Gonzales et al. 2003; Tierney 2003). Authorities who fail to disseminate the relevant information, or who misrepresent it, add to the collective distrust of authority and undermine their own abilities to influence behaviors.

While the public reaction is not likely to be one of blind panic, there are indications that the public may not always cooperate with instructions they would likely receive in the event of a bioterrorism incident. Sometimes the public response does not seem to be entirely rational. Lasker (2004) found that only 24% of the population would immediately comply with a recommendation to report to vaccination centers in the event of a smallpox outbreak. Confused by their knowledge of pre-exposure vaccination risks and benefits, the respondents were unable to compare these with the risks and benefits of post-exposure vaccination. The majority of the population (55%) said they would wait and collect information about whether or not to seek the vaccine. Identifying and addressing such public information needs beforehand will clearly aid in the timely and effective execution of a response. This is the kind of situation where timely and focused risk communication could decrease adverse outcomes (i.e., increase the number of people protected by the vaccine).

Non-cooperation with instructions is not always a matter of public misperception. In some cases the personal and societal goals are truly divergent. There are both private risks and aggregate (societal) risks and incentives for risk mitigating behaviors. When the incentives are aligned, the individuals act in accordance with the public good. When they are not, the individual may chose behaviors that increase societal risk. Examples of this from recent events include the 1994 pneumonic plague outbreak in Surat, India. Half a million Suratis fled that town within one week despite government efforts to restrict travel(Garrett 2000). Another example was the refusal of some healthcare personnel to treat SARS patients during the Toronto epidemics (Singer, Benatar et al. 2003; Straus, Wilson et al. 2004) out of fear for personal safety or the safety of their families. In such cases, strategies to harmonize incentives may be more successful than simple provision of information.

In some cases, public non-compliance with governmental directives may be justified. The federal program to vaccinate half a million healthcare workers and emergency responders against smallpox terminated well short of coverage goals. Once the previously unknown linkage between heart attacks and smallpox immunization became known and bioterrorism fears

decreased with the fall of Saddam Hussein (McNeil Jr. 2003), the national plan stalled at fewer than 40,000 vaccinations. The rationale for rejecting pre-exposure vaccination was formalized in risk analytic terms by Meltzer who concluded that for a healthcare worker to accept pre-exposure vaccination, the risk for contact with an infectious smallpox case-patient must exceed 1 in 100 and the probability of there being more than 1000 initial cases must exceed 1 in 1000 (Meltzer 2003). The mental calculus of the health care workers was informal, but it arrived at the same conclusion: "reject pre-exposure vaccination until the perceived risk is large".

Public perceptions of the risks of bioterrorism and of mitigation actions impact their compliance with response measures and ultimately impact the success of the mitigation efforts. Clearly there are many possible divergences between governmental response plans and public responses to bioterrorism. Better understanding of these divergences and of ways to remedy them is essential for the development of effective response plans to bioterrorism incidents. However, systematic research is needed to achieve this improved understanding.

A. Analytical Framework

This research will apply the "mental models" research approach to understanding bioterrorism risks (Morgan, Fischhoff et al. 2002). The mental models approach uses the following procedure to understand public perceptions of technological risk:

(1) Determine the knowledge most relevant to predicting the outcomes that matter most to citizens and formally represent this knowledge in an influence diagram.
(2) Empirically, determine what citizens know already.
(3) Identify the most critical gaps[3]

In the mental models approach, people's understandings of risks are revealed using open-ended interviews and survey questions. The lay understanding, or "mental model," is then compared to a model of expert understanding. Identifying where the lay model differs from expert understanding helps to identify the risk communication needs.

The spectrum of potential bioterrorism incidents is wide. In keeping with the overall framework of this project, a limited number of scenarios will be explored in detail. The scenarios considered in Objective 2 will be a limited number of scenarios drawn from the set of scenarios developed in Objective 1. While it is possible to recalculate numerical models of exposure and risk numerous times with different input parameters, eliciting information from the public is a labor-intensive process. For this reason it is expected that only two scenarios will be considered here. While the exact choice of scenarios will depend on the results of Objective 1, one of the scenarios is expected to focus on post-attack building decontamination of anthrax. This scenario is of interest because no level of decontamination can guarantee zero re-occupancy risk. Workers may be asked to accept vaccination or to reduce their risk of future infection by some other method as part of a reoccupation plan. Given recent reactions to government plans for bioterrorism preparedness, it would be foolish *a priori* to assume complete compliance. Plans

[3] The full mental models approach usually includes the development and testing of risk communication instruments for the specific audience. This phase is not part of the current proposal.

that extend to family members may be greeted with even more skepticism. Workers or other stakeholders must perform a mental risk-risk comparison before deciding on a course of action. Our research will explore the public perception of re-occupancy and risk management plans in an attempt to identify their most pressing information needs.

The second scenario is expected to involve the widespread release of a transmissible pathogen, such as smallpox or a novel genetically modified pathogen. Many of the same issues considered in the first scenario will be considered here, such as willingness to comply with governmental instructions, and the need for an informed risk-risk assessment of personal choices. In addition, this scenario may involve quarantine measures, voluntary isolation, the distribution of prophylaxis, the closure of places of public assembly (including schools), etc. The public perception and response to these measures will be assessed. Perceptions of members of the medical and emergency response communities will also be studied.

B. Project Outline

a. Development of the Expert Model and Influence Diagram

In order to conduct a behaviorally realistic risk analysis, our research process begins by creating a formal model of the processes creating and controlling specific risks. An example of this kind of analysis is found in Casman, Fischhoff et al. (2000). These models use the formalism of *influence diagrams*, which levels the playing field for contributors with different forms of knowledge, while still demanding the sort of rigorous thinking needed to reveal interactions, ambiguities, and uncertainties. CAMRA researchers in collaboration with outside experts, will construct influence diagrams of the factors contributing to the risk of the two bioterror scenarios. In addition to the usual release, fate, transport, exposure, and consequence features, these models will include concepts usually absent in risk assessments, such as control/mitigation strategies, time dependencies, feedbacks, heterogeneous populations, sensitive/sentinel populations, host immune status, information development and flow, monitoring results, technological constraints, individual choices in risk taking/avoidance behaviors, and institutional governance. For potential zoonoses (like plague) the diagrams will also include disease dynamics in animals and insects, interactions with humans, and control efforts aimed at animal hosts. The diagrams serve as outlines onto which public perceptions can be mapped and compared.

b. Identify affected population sectors

The mental models analysis identifies the knowledge crucial to informed lay person decision making. However, sectors of the public face different risks and have different reactions to the risks because of occupation, age, immune status, familial obligations, or other factors. Thus, the information needs are likely to differ by target populations, reflecting the different decisions that they face. For example, first responders may need to know specific details about the most directly impacted sites, allowing them to prioritize their actions; the general public may need to know more broadly which segments of society are affected in what ways, allowing them to make

the best sense of their circumstances, to interprets officials' recommendations, and to identify personally relevant choices; individuals with certain medical conditions may need to understand yet a different set of details to enable them to compare the personal risks of action and inaction.

c. Information needs

Communication needs are determined by the gap between what people know and what they need to know. Incorrect assumptions regarding people's beliefs may result in the failure to deliver needed facts in a comprehensible way, and can also undermine communicators' credibility. Providing information that people already grasp will lose their attention, while providing guidance that cannot be understood without a necessary baseline of knowledge can result in the guidance being misconstrued or ignored. This procedure described here is a systematic effort to avoid these pitfalls.

The first step in this procedure is to identify critical decisions. The influence diagram will be reviewed and important decision variables identified. These may include personal decisions, such as seeking medical care, complying or not complying with governmental instructions, and institutional decisions such as when to issue warnings to the public, when to alert federal authorities, whether to mobilize drug stockpiles, what disinfectants to use, whether to institute pest control, when to institute quarantines and to whom they should apply, whom to treat, and how to handle triage of potential victims. This information will be used to inform Objectives 1 and 5, to make sure the models properly incorporate the significant social variables. It will also narrow the focus of the analysis by identifying where decisions lead to risk relevant actions.

The next step is to assess the baseline knowledge of the target group concerning factors that would influence these critical decisions. For important population subgroups, we will conduct open-ended, semi-structured interviews, allowing individuals to express their own ideas in their own terms. This will allow us to ascertain how the public frames the problem. Interviews will be taped, transcribed and coded according to their relationship with the influence diagram. This is an objective way to represent baseline public knowledge and attitudes which will allow for the systematic identification of gaps between the expert model and the lay understanding.

The comparison of the interviews and the expert model will also offer an opportunity to identify situations where public and private incentives are in variance. All such situations encountered in the interviews will be recorded and a summary list developed. In these circumstances, measures beyond risk communication may be called for, such as the provision of appropriate incentives to bring the private and public interests into line. The identification of these situations by this research project will thus provide a basis for subsequent research into the design of response plans that reconcile public and private incentives.

d. Construct list of risk communication priorities

The knowledge gaps identified by the analysis of the semi-structured interviews will then be prioritized. Not all misinformation is equally important to risk; the goal will be to identify those information gaps that adversely affect critical decisions, so that these misconceptions may be targeted for future risk communication efforts. Thus, the end product of this task will be a list of key elements to include in communications with the public.

This list of communication needs will inform both pre-event public education programs and post-event contingency plans. Fundamental misconceptions are best addressed before the event, given the limited timeframe and potential communications difficulties expected in an attack. However, an analysis of pre-event knowledge and understanding will serve also to identify the public concerns likely to lead to non-compliance with governmental risk management plans and allow the design of post-event response plans that address these concerns.

e. Integrate with other CAMRA research activities.

By illuminating the connection between public perception, behavior, and risk, this project has the potential to improve the practical usefulness of the results derived in other CAMRA projects. Systematically identifying behaviors that potentially increase or decrease personal risk will permit these behaviors to be included in risk models (Objective 1). Behavioral choices represent an element of uncertainty in risk assessments, and explicitly incorporating them in the risk analysis gives a more realistic idea of the range of outcomes (Objective 3) including behaviors that affect secondary transmission (Project II). This task will identify instances where the possession or absence of information influences risk. The value of such information can be quantified (Objective 4). Lastly, information on public risk perception and attitudes forms an important component of the educational curriculum of Project V that will help train risk managers in how to interact with the public

Objective 3. Development of Probabilistic Descriptions of Uncertainty and Relatedness
Probability distributions will be developed to describe the uncertainty of input parameters with the potential to contribute substantially to model output uncertainty. The potential of various inputs to contribute to uncertainty in model outputs will be assessed by the literature review (described above), and the uncertainty/sensitivity analyses planned for the other CAMRA projects. Thus the literature review for fate and transport models will be conducted jointly with researchers on Project I and important uncertainties identified by Project I researchers will be included in the integrated assessment of this Project. An analogous process will be conducted with researchers from Project II (for secondary transmission models) and Project III (dose response models). All of these activities will be coordinated with Project V in order to identify key inputs for the knowledge and data repositories. It is expected that some input parameters will be fairly well defined (for example the dispersion coefficients for atmospheric transport under a given weather scenario) and may appropriately be described by point estimates. Many

other parameters will be subject to substantial uncertainty (e.g., the dose-response functions for cutaneous anthrax and smallpox, Raber et al. 2001) and this project will seek to appropriately quantify the uncertainty in these estimates.

Quantifying uncertainty in the domain of bioterrorism presents great challenges going far beyond issues of sample variability. For obvious reasons there is little information on the infectivity and environmental persistence of many bio-threat agents (Raber et al. 2001). It is common practice to use surrogate information where needed to fill in the inevitable data gaps in a risk assessment. For example, dose-response data from animal models are commonly used in place of human dose-response data. Unfortunately, classical statistical descriptions of uncertainty fail to provide useful information in such cases. In the classical framework, the surrogate information is considered either completely representative of the quantity of interest or completely irrelevant. Bayesian hierarchical approaches provide a means to share information among related model parameters and even develop estimates for model quantities that have not been directly observed. In this framework, the parameters of the prior distributions describing initial uncertainty in the model parameters are viewed not as fixed values, but as random variables drawn from hyper-distributions. Parameters that are intrinsically related are modeled as deriving from the same hyper-distribution. For example, estimates of the dose-response model parameters for an infectious agent may be available for a variety of non-human animals, but a prediction and assessment of the uncertainty in the human value is required. The first stage of the model would be to specify a prior distribution for the model parameter of interest. For example, the r parameter from an exponential dose-response model could be modeled as:

$$\mathrm{Ln}\,(r_i) \sim N\,(\mu, \sigma^2)$$

where i is a subscript referencing species type, and μ and σ are the mean and variance of the distribution of r values across different species. Prior distributions for μ and σ are specified by the second stage of the model:

$$\mu \sim N\,(M, S^2)$$

$$2\,\mathrm{Ln}\,(\sigma) \sim N\,(m, s^2)$$

where M, S, m, and s are fixed hyper-parameters. In this manner, observations of r values for non-human species may be used to update estimates of μ and σ^2 and the resulting informed estimates of μ and σ^2 used to develop a predictive distribution of r for unobserved species. Hierarchical modeling techniques are well established in the statistical literature (see Lockwood et al. 2001 for an example application). Previous researchers in the field of microbial risk assessment have developed hierarchical models of the variability of infectivity among *Cryptosporidium* strains (Messner et al. 2001, Teunis et al. 2002). These approaches are well suited to bio-threat agents for which there is often little direct experimental data on a wide range of characteristics including infectivity, persistence in the environment, and susceptibility to disinfectants, but where information on surrogate organisms or hosts may either be currently available or much more feasible to collect.

Objective 4. Value-of-information calculations

Prioritizing among different research needs is a difficult task that involves balancing many different factors, such as:

- the extent of uncertainty in a given model parameter,
- the sensitivity of key model results to uncertainty in this parameter, and
- the potential for reduction in uncertainty in the parameter as a result of future research efforts.

For example, the quantity of a bio-threat agent that is released is likely to be a highly uncertain variable, and model results are likely highly sensitive to this variable. However, this would likely not be a promising area for future research because the release quantity depends on the capabilities and knowledge of terrorist organizations, topics for which additional research is unlikely to substantially reduce uncertainty. In contrast, the transport of bioterrorist agents, including their re-suspension into indoor air and susceptibility to different disinfectants is in many cases still uncertain. In this case, the parameters in question can be measured in laboratory experiments, and a carefully designed research program has to potential to make real contributions to reducing the uncertainty in model predictions.

Given the inherent complexities of the task, effectively prioritizing among different research efforts requires a formal approach. Value-of-information calculations, an established decision analytic technique (Clemen and Reilly 2001), provide such a means of prioritizing among different research efforts. In this approach, uncertainty distributions are fit to key model parameters. In addition, probability distributions are developed that reflect the reductions in uncertainty obtained by additional research. In cases where preliminary data exists and one is simply augmenting the sample size, these distributions can be developed by Monte Carlo simulations of the sample information obtained. In cases where the research track is entirely novel, then it may be necessary to rely on subjectively elicited distributions of the value of the research results despite the cognitive and motivation biases to which such procedures may be subject (Morgan and Henrion 1990). In cases where subjective judgments are required, a variety of experts not associated with CAMRA will be recruited (similar to the procedure followed by Morgan and Keith 1995) and elicitation procedures designed to minimize biases will be employed (Morgan and Henrion 1990, such procedures expected to diminish but not eliminate biases).

A decision problem will be constructed to model the options available to risk managers and the likely outcomes of their decisions both with and without the information provided by the additional research. Informed in part by the public preferences elicited as part of Objective 2, a utility function will be assigned to a key model output (or potentially outputs). The valuation of the information provided by the research will be assessed by the differences in the expected results of the scenarios with and without the information gained from the additional research (Clemen and Reilly 2001). An important feature of this valuation approach is that future research will be valued not directly for the reduction in scientific uncertainty achieved (an attribute perhaps more valued by researchers than by the public) but by its relevance for aiding risk managers in deciding between the alternative risk management strategies to meet public goals and expectations.

Alternative allocations of research effort may then be proposed, based on either the investigators' intuition or using formal optimization techniques, and the most promising allocation identified. The proposed work will be, to the best of our knowledge, the first application of this approach to prioritizing research needs in the bioterrorism field and one of few attempts to apply this methodology to such a complicated set of interrelated models (see Dakins et al. 1996 for an example of applying value-of-information calculations to environmental remediation efforts).

A priority will be to produce initial results in a timely fashion, such that useful input may be given to the teams responsible for the other projects. For example, the results may help researchers on Project I to identify whether better knowledge of sensitivity to disinfectants or better knowledge of re-suspension rates would be more useful to inform risk management decisions. To this end, initial results will be available by the end of the second year in order to have time to substantively influence CAMRA's own research program.

Objective 5. Implementation of results and iterative refinement of calculations
The initial results described in Objective 4 will of necessity not be definitive. Instead, the analysis will be conducted in an iterative fashion with successive refinements adding details to the evaluation, expanding its scope, and incorporating the latest assessments of the appropriate underlying modeling techniques and parameter uncertainties. This strategy of iterative analysis can be considered a best practice for complicated decision and risk analyses that can never be performed in a definitive fashion but do benefit from the attempt to address them in a systematic, quantitative fashion (Morgan and Henrion 1990). Alternative model formulations, particularly alternate valuations of uncertainty reductions, will be pursued throughout the project in order to elucidate how their assumptions affect the conclusions and recommendations of the evaluation.

3. Expected Results and Benefits

This project is an ambitious attempt to understand and inform the societal response to bioterrorism risks. It will result in the creation of a novel and sophisticated decision model to understand bioterrorism impacts, assess uncertainties, and prioritize research efforts. However, the goal is not model building for its own sake, but the creation of a set of key information summaries as outputs:

- A compilation and systematic representation of expert knowledge related to bioterrorism in an influence diagram (Objective 2).

- A list of risk communication priorities for both pre-event public education and post-event response plans (Objective 2).

- The identification of situations where public and private incentives are in conflict (Objective 2). This will provide a basis for the design of response strategies that harmonize these incentives.

- The identification of key knowledge gaps and the prioritization of alternative research plans (Objective 4).

These results will provide practical guidance for important risk management decisions that must be made in preparation for and in response to a bioterrorism event.

4. General Project Information

4.1. Personnel

This project will bring together a diverse team with backgrounds in microbiology, cognitive psychology, Bayesian statistics, and environmental modeling. Brief summaries of the expertise of key personnel are provided here.

Mitchell Small is the H. John Heinz III Professor of Environmental Engineering. Jointly appointed in the Departments of Civil & Environmental Engineering and the Department of Engineering & Public Policy, his expertise includes mechanistic and statistical environmental modeling, Bayesian methods in environmental decision making, and behavioral models of exposure. He is the chair of EPA's Science Advisory Board's Environmental Models Subcommittee, was elected a Councilor of the Society for Risk Analysis, and has served on five National Research Council committees.

Elizabeth Casman is a research engineer in Carnegie Mellon's Department of Engineering and Public Policy. She holds graduate degrees in Microbiology (M.S.) and Geography and Environmental Engineering (Ph.D.) and has worked extensively on integrated assessments of human diseases, including malaria and cryptosporidiosis, and is currently involved in an NSF-sponsored study of the human and social dimensions of risk from intentionally released *Yersinia pestis*. She is also interested in bioterrorism early detection technology and policy, and is studying the feasibility of various early detection strategies under the sponsorship of the MacArthur Foundation.

Patrick Gurian is an assistant professor in Drexel's Department of Civil, Architectural, and Environmental Engineering. He holds a doctoral degree in Engineering & Public Policy and Civil and Environmental Engineering from Carnegie Mellon University. His previous research experience includes the use of Bayesian statistical methods to develop an integrated assessment of drinking water risks and risk management options. His current research projects include an NSF-sponsored study of extreme-event risk to the U.S.-Mexico border crossing infrastructure and an application of the mental models approach to communicating the risks of carbon monoxide poisoning.

Julie Downs is the director of Carnegie Mellon's Center for Risk Perception and Communication. Her doctoral degree is in Psychology, and she has over a decade of experience researching human perceptions of risk, including previous applications of the mental models approach to the development of a risk communication instruments. Her research has identified the role of stigmatization in influencing human responses to the risks of transmissible diseases.

4.2. Project Organization

This project will be a joint effort of Drexel and Carnegie Mellon that is closely integrated with the work of other CAMRA researchers. Elizabeth Casman, Mitchell Small, and Patrick Gurian

will collaborate on Objective 1 (identification of scenarios and modeling tools) using a consultative process involving input from a wide range of CAMRA researchers, including the steering committee and the lead investigators on the other four CAMRA projects. Coordination with Projects I-III will ensure that this Project uses appropriate models for fate and transport, secondary transmission, and dose-response, respectively. Coordination with Project V will ensure that appropriate information is identified for the knowledge and data repositories. The coding of an integrated model will be performed by a Drexel doctoral student under the supervision of Patrick Gurian.

Carnegie Mellon will have primary responsibility for Objective 2. Elizabeth Casman will direct the development of an appropriate expert model and influence diagram, and Julie Downs will direct the public perception research. Subjects will be recruited by a subcontractor specializing in public opinion research and interviewed over the telephone by Carnegie Mellon researchers.

Patrick Gurian will have primary responsibility for Objectives 3 and 4. Elizabeth Casman and Mitchell Small will assist with the development of probabilistic descriptions of uncertainty and the value-of-information calculations. The selection of key model input parameters and appropriate uncertainty levels will be coordinated with researchers on Projects I-III. Coordination with Project V will ensure that key information identified during this task will be incorporated in the knowledge and data repositories. Model coding and implementation will be performed by a Drexel graduate student.

The iterative refinement of the model (Objective 5) will be directed by Patrick Gurian in consultation with Elizabeth Casman, Mitchell Small, the steering committee, and other CAMRA researchers. Input will be sought from other CAMRA researchers as to the appropriate priorities for improving the scope and detail of the model (i.e., Project I researchers would provide input on appropriate refinements to the fate and transport modeling effort, etc.). These refinements may involve the incorporation of novel results from other CAMRA projects, such as the elucidation of better dose-response models from Project III.

4.3. Schedule

The activities of this project are concentrated into the first three years with the goal of having preliminary results available within the first two years. This will allow the priorities established by this research to influence CAMRA's own research prioritization. Figure IV.1 shows the project timeline. Objective 1 involves initial tasks to define the scope of the analysis, such as the development of attack scenarios, selection of appropriate modeling tools, and coordination of scenarios and models with other CAMRA projects and will be completed in the first year.

Figure IV.1. Project Schedule

	Year 1	Year 2	Year 3	Year 4	Year 5
Objective 1					
Objective 2					
Objective 3					
Objective 4					
Objective 5					

Work on public perception (Objective 2) will also begin in the first year, including the pilot testing of an interview protocol, the identification of relevant population segments, the recruitment of subjects, and the first set of interviews. In the second year, the remainder of the interviews will be completed, transcribed, and coded, and the analysis of the results will commence. The analysis of the results will continue into the third year and efforts to disseminate the results will begin. This will include the preparation of a journal article on the findings as well as informal communication with other CAMRA researchers through the development of an educational program (Project V) and steering committee meetings.

Work on Objective 3 will begin in the first year, as soon as sufficient progress has been made on Objective 1 to define the required model inputs. Objective 3 is scheduled to be completed by the end of the second year in order to allow preliminary value-of-information calculations (Objective 4), beginning in the second year and becoming successively more refined throughout the third year. By the third year all the major pieces of the analysis will be in place and the emphasis will switch from building the modeling framework to iterative refinements of the framework (Objective 5) and dissemination of results informally through the CAMRA steering committee and formally through journal publications and contributions to the educational curriculum of Project V.

4.4. Facilities

All researchers associated with this project have fully equipped private offices with personal computers and the requisite software, including C-language compilers, Matlab, R, Analytica, SPSS, etc. Graduate student computing resources at Drexel include a dual processor Pentium computer.

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Project V. Knowledge Management, Transfer, and Learning
Leads: Dr. Rosina Weber & Dr. Ewen Todd

1.1 Objective:

The understanding of elements involved in microbial risk assessment (MRA) (Haas et al. 1999) and how they relate to each other as a body of knowledge has several societal benefits, particularly concerning development of a biosecurity plan and an increase in the safety regarding the quality of food and water. It is the overall objective of this project to investigate and implement effective and efficient methods to enhance the understanding of microbial risk assessment as a body of knowledge. For this purpose, we focus on education and collaboration in combination with technological methods to promote and leverage the management, transfer, and learning in this still novel field of study.

There are several communities that can benefit from the knowledge in microbial risk assessment. Each having different purposes, backgrounds, and playing distinct roles in the process of learning about microbial risk assessment and applying its knowledge for improving the health, preparedness, and safety of our society. The first is the community of scientists involved in the various aspects of the evolving field of MRA, including the core of CAMRA. The second is the public who has an interest the tools, information and application of MRA to their respective fields including policy makers, DHS members, EPA members; technicians and managers in federal agencies, department of agriculture, health, education, energy, and defense. The final community is that of students in which the education of the next generation of microbial risk assesssors will be undertaken. The efforts to reach these communities in this project are categorized as technologically-oriented -- Technological Knowledge Management, Transfer, and Learning (TKM), public-oriented –Communication CKM and finally education-oriented – Educational (EKM).

The overall goal is to provide effective and efficient technological support for group collaborations, that result in a knowledge repository linked to a data repository, where knowledge can be discovered and leveraged, helping to advance different fields of study including programs in higher education and outreach to the community of professionals. This will include the ability to develop various science and knowledge-based approaches for integrating the type of data, mathematical models, tools and other variables for the advancement in the science, communication and educational programs for MRA..

Specific Objectives:

1. The Technical Knowledge Management, Transfer and Learning for CAMRA
1a. . Build an online repository based on evolving learning units.
1b. Reason with learning units for knowledge discovery.
1c. Build a data warehouse from data linked to the learning units.
2. The Communication Knowledge Management, Transfer and Learning for the Public.
2a. Develop CAMRA website and other means of dissemination.
2b. Develop a series of workshops for professions who will utilize the MRA frameworks (eg.. to develop recommendations for policy to reduce the risk of transmission of select and other agents to populations in the U.S.)
3. The Educational Knowledge Management, Transfer and Learning for Students.
3a. Develop targeted courses (on-line)

3b. Develop summer workshop for graduate students and post-graduate associates

1.2 Technological Knowledge Management, Transfer, and Learning (TKM) for CAMRA

Collaboration is key to learning and sharing. It is how groups find data, understand information, and create knowledge. This project focuses on managing learning for the Center for Advancing Microbial Risk Assessment (CAMRA). CARMA scientists are dispersed across the country, posing the need for technological support for collaboration among its members. Because its members share the same general goals and interests, CAMRA is a community of practice. The domain-specific artifacts in collaborations among CAMRA's members should be easily accessible to all group members. Data repositories create challenges for effective retrieval and may hide valuable knowledge. Knowledge repositories are difficult to create and validate. How to support distributed group collaboration that results in data and knowledge repositories is not yet well understood. When knowledge learned through group collaboration is lost, the value of data is diminished and advancements are slow. An effective methodology to support group collaboration that facilitates the semi-automated creation of knowledge in association with existing data can significantly leverage knowledge in a field and promote its sharing throughout a large population.

Our long-term goal is to provide effective and efficient technological support for group collaborations, that results in a knowledge repository linked to a data repository, where knowledge can be discovered and leveraged, helping to advance different fields of study. In this project, we will implement a collaborative framework that will support the semi-automated creation of a knowledge repository linked to a data warehouse in the MRA domain for the CAMRA community. The knowledge repository will retain data in units of knowledge, henceforth referred to as *learning units* (LU). LU adopts a general knowledge representation formalism that can be further tailored. We will study the submissions of LU by CAMRA members to investigate its evolution into a specific format that is suitable to the MRA domain. This knowledge representation is based on lessons-learned (LL) (Weber, Aha, Becerra-Fernandez 2001). Lessons-learned have been defined in different industries (id.) as a knowledge artifact that teaches how to perform a task in an effective way. Our central hypothesis is that using an task-driven LU as the central instrument of collaboration will facilitate the creation of integrated knowledge and data repositories that promote knowledge leveraging and sharing. This hypothesis originates from the recognition that usefulness stems from the applicability of a piece of knowledge and that members are motivated to contribute when they see the value of their effort.

In order to further motivate CAMRA members, the PI of the TKM project will visit all CAMRA sites to educate its members on the benefits of using the repository. This is expected to bring them the understanding required to motivate contributions.

The development of a collaborative framework centered on an task-driven LU will result in a knowledge repository where more knowledge can be discovered and used in reasoning. The integrated data repository can also be used for knowledge discovery, as well as to build a database for public access. The explicit usefulness of LUs facilitate knowledge retrieval,

promoting knowledge sharing and leveraging. The systematic representation of the associations between knowledge and data will represent a framework for browsing that will also promote sharing.

The knowledge repository will promote knowledge sharing and leveraging in two ways, as a powerful knowledge repository and also in collaboration aspects of its construction. The automated methods will help uncover unknown knowledge and inconsistencies between LUs, becoming yet other sources of knowledge sharing. Finally, the data warehouse will be made available to the remaining communities interested in MRA, and provide another platform for knowledge discovery.

Given the aggregating role of this project, it interrelates similarly to all the remaining projects in this proposal. All leads and personnel working in all projects will be users of the knowledge repository. The TKM component is complementary to the EKM component (detailed later in this description). The understanding produced by the educational efforts in EKM will be used in the design of the repository's task network and data warehouse. Project Four can immediately benefit knowledge learned as automated methods may reveal gaps in MRA knowledge, which can be investigated in Project Four.

1.2.1 Approach: TKM

Background

Knowledge management initiatives refer to knowledge repositories, knowledge access and transfer, and knowledge environments (Davenport and Prusak1998). Our focus is in the use of computational methods a repository's storage and retrieval. Repository-based KM initiatives were surveyed by Weber, Aha, and Becerra-Fernandez (2001). KM repositories are distinguished by the knowledge artifact (Holsapple and Joshi 2001) they retain. They found the most widely used knowledge artifact was lessons-learned, whereas probably the most popular are best-practices. One of the conclusions from this survey was that these systems posed challenges for their users, resulting less effective than desired. Further study of technological, human, and managerial issues involving the use of lessons-learned systems have indicated a number of requirements that organizations and the supporting technology have to respect (Weber, Breslow, Sandhu 2001). The study of collaborative learning (Stahl 2003) recommends design strategies for the organizational and technological support of successful knowledge sharing.

The definition for LL evolved from different industries that adopted lessons-learned systems (Weber, Aha, Becerra-Fernandez 2001). To be considered lessons-learned, the knowledge artifact must include the specific task or process where it can be reused and the embedded lesson has to guarantee a positive impact to the targeted process. After addressing specific technological impediments for knowledge sharing, Weber and Aha (2003) proposed a knowledge representation formalism for LL. This formalism enforces that LL requirements are met. The representation formalism for LL originated from the development of a methodology for the active distribution of lessons-learned (Aha et al. 2001). This methodology – monitored distribution (MD), relies on analogical reasoning for retrieving lessons. The underlying reasoning methodology that supports analogical retrieval is case-based reasoning (CBR) (Kolodner 1993, Aha 1998). CBR is a reasoning methodology inspired by the human process of remembering a previous episode to solve a similar new problem. The act of being reminded of a previous episode is modeled in case-based reasoners by comparing a new problem with a collection of stored cases (the "case base"),

often based on indices describing the contents of the stored cases. The most similar cases are then retrieved, and the solutions from the retrieved similar case(s) are adapted to fit the new problem. A case-based reasoner stores situated experiences (cases) of performed tasks in a case library. Cases describe performed tasks by having a description of a problem, a solution, and the result of applying the solution to the problem. Given the commonalities between cases and LL, their representation is mainly composed of three sub-modules: indexing components, reuse components, data components. Indexing components are responsible for facilitating retrieval; reuse components allow the lesson's reuse; whereas data components keep track of a lesson's use. The LU being proposed in this project is based on this lesson representation formalism. The direct benefit of using such a knowledge representation formalism is that it enables analogical reasoning. Other uses of computational intelligence methods have been suggested for repository-based KM systems. The survey of intelligent lessons-learned systems (Weber, Aha, Becerra-Fernandez 2001) describes some uses, which include knowledge validation and learning.

In fact, adopting a formalism that allows the application of a reasoning methodology such as CBR extend the availability of all techniques developed for CBR to the repository that retains LUs. Some examples of these methods refer to knowledge acquisition and maintenance. Another use of a CBR system is exemplified by CARMA (Branting, Hastings, Lockwood 2001). CARMA is designed to provide expert advice on handling rangeland grasshopper infestations. CARMA helps users to devise policies on pest management and the development of industry strategies. Within knowledge maintenance methods that have been devised for CBR and that can be directly applied to leverage our understanding of a knowledge repository is the use of genetic algorithms (GA) (Craw, Jarmulak, Rowe, 2001.) and neural networks (NN) (Shiu, Wang, Yeung, 2001).

One approach that is useful in immature domains, consists of extracting domain knowledge for a task such as classification and then examine how well the existing experiences can successfully classify new problems in comparison to domain knowledge. Weber et al. (2003) applied a parameterized function that combines CBR with explanation-based learning (Cain, Pazzani, Silverstein 1991) to perform classification. Then, Weber et al. (2004) investigated methods to identify variations in data that could reverse a classification. The resulting predictions pointed to inconsistencies, new knowledge, and new questions.

A data warehouse (DW) is an environment that facilitates effective integration of traditional databases into an infrastructure that enables strategic use of data (Berson and Smith, 1997). A multidimensional database is required to overcome limitations of the traditional relational databases (Kimball and Ross 2002). Multidimensional databases can easily perform elaborate and complex queries by being coupled with On-Line Analytical Processing (OLAP) (Kimball et al. 1998; Pedersen & Jensen 2001).

Goal 1: Build an online collaborative repository based on evolving learning unit

Introduction. This project targets CAMRA's community members, who are scattered throughout the country. To support their collaboration and learning needs, we will build a knowledge repository (KR) centered around an evolving learning unit (LU) that identifies the task where it can be used. We expect to deliver a platform that will effectively promote knowledge leveraging and sharing among CAMRA members. This is an important element particularly in a novel domain like MRA where knowledge is scattered, sparse, and mostly

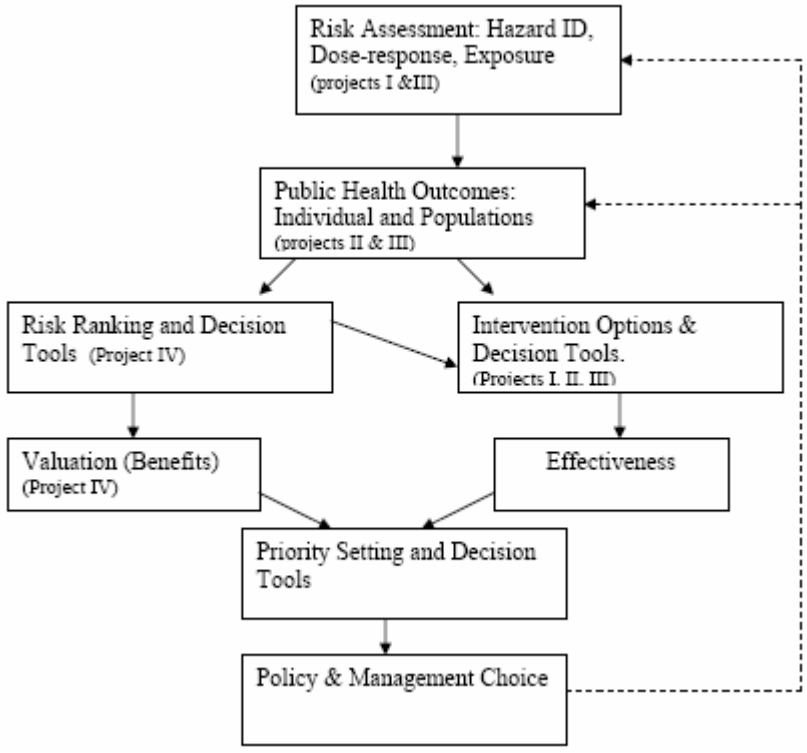

Figure 6. Addressing and Controlling Biological Agents

implicit. The construction of this knowledge repository is critical to the advancement of the field of MRA and it also contributes to the fields of knowledge management and knowledge-based systems. Design. The knowledge repository (KR) will be built by all CAMRA scientists. Dr. Rosina Weber will visit every CAMRA institution to explain and educate CAMRA scientists about the use of the KR. We will build the KR using group collaboration principles. The KR will rely on an evolving LU. A hierarchical task network will organize the LU structure.

We will visit CAMRA's members to educate them on how to use the KR about the potential benefits of using it in order to motivate their contributions. This education aims at motivating the community to collaborate by demonstrating the potential return to their own knowledge productivity, which is to be made transparent. Community members will be prepared to understand the goals of the knowledge repository and to understand all its operational processes. All members will be encouraged to provide feedback to guarantee that the use of the KR is always beneficial. We will primarily focus on the understanding of the purposes of the repository because it is understood that members will not contribute to knowledge management efforts unless their benefits are transparent and perfectly understood.

Following group collaboration principles, scientists will be free to submit contributions in various privacy levels. Group submissions will be supported. We will encourage users to document their communications so we can use this data for further understanding. Access history is stored through log data for each access.

We will have a knowledge engineer examining the evolution of the repository and the particular adaptation needs for the LU to adjust it to the domain of MRA and CAMRA's members. After the LL concept, LU must identify its applicable task, in which it can be applied. We want to determine the specific elements in the LU considered ideal to represent knowledge in the MRA domain that meets the needs of CAMRA scientists. Members of the community will be allowed to add and recommend variations to the learning unit until we observe a reduction in the need for changes. For a scientific community, one element is the rationale, stating the scientific grounds supporting a LU (e.g., literature, statistical analysis).

A task-oriented formalism can improve the recall levels of retrieval but it is also beneficial to allow members to browse through these tasks. For these purposes, it is necessary that knowledge workers study the application domain for maintaining a hierarchical task network

(HTN). A knowledge engineer will study the structure of the HTN by finding associations between different tasks described in the LU. Figure 2 shows the framework of processes for studying biological agents. These relationships between processes imply relationships between specific tasks, which will be covered in the HTN.

Hypothesis and Evaluation. Our working hypothesis is that this knowledge repository will promote knowledge sharing and leveraging throughout CAMRA's community. We will evaluate such hypothesis by recording the LUs that have been submitted by distributed members, LUs that have been submitted by one member and modified by other, and LUs that have been submitted by one member and then linked to another LU by another member.

Goal 2: Reason with learning units for knowledge discovery

Introduction. Technological support for knowledge management goes beyond the support for group collaboration. This goal will be met by using automated methods to promote further knowledge learning. Our hypothesis is that we can discover knowledge in novel ways because our repository will have database records that represent knowledge. There are several ways to uncover knowledge from data records, but those do not explore the implied association within a piece of knowledge, i.e., a record that describes a task in a given context. The approaches we will adopt rely on computational intelligence (CI) methods, e.g., genetic algorithms (GA) and neural networks (NN). Because the learning unit is represented with a framework amenable to case-based reasoning, all methods developed for the CBR methodology can also be used in the knowledge repository. These studies will uncover knowledge and gaps in knowledge that would be hardly attainable by humans or when using traditional databases.

Design. Learning algorithms such as GA and ANN can help us understand the knowledge repository by identifying similarity measures, relative weights representing the importance of distinctive features in a learning unit, redundant units, and representative units.

Given the importance of the HTN, which includes browsing and reasoning, CI methods can be applied for its validation as well. Additionally, the use of inductive logic to learn structures in data may lead us to uncover other relationships that have not yet been captured.

To use the repository for reasoning, we will define measures to assess similarity between LUs. Given a cluster of LUs that share similar problems, it is possible to select a library of units to perform reasoning tasks. For example, a classification task can be performed for identifying consistency of units describing experiences and formal domain knowledge. The result can be the uncovering of knowledge previously unknown and also the identification of research questions. Some of these questions will be used to guide the design of the data warehouse in the following goal.

Hypothesis and Evaluation. Our hypothesis is that a repository whose records meet criteria of a knowledge representation formalism can be used for reasoning tasks. We evaluate such a hypothesis by comparing the results we obtain with our methods on our repository's LU with results obtained in a database that does not use the LU's representation formalism.

Goal 3: Build a data warehouse from data linked to the learning units

Introduction. The knowledge repository is limited to CAMRA members. However, it is necessary to make all the data gathered in the process of building the knowledge repository available for all the communities involved with MRA. Once all this data is organized in a data warehouse (DW), it can be made available online and yet additional knowledge can be discovered with the use of data mining algorithms. The resulting format of the LU will have data sources linked to one to many of its sub-components. For example, the LU's rationale may have links to files and online links. This objective will be attained by the design and development of a DW, which will take into account the structure of links between the data and the KR, means for updating the DW to follow up with the growing of the KR, and the design of methods for knowledge discovery from data.

Design. The DW will be designed with three-tier architecture residing on a server at Drexel University. The first tier consists of various data sources that are geographically distributed in the US. The middle tier consists of data conversion and model conversion. The third tier is web-based interface. Our data warehouse (DW) is connected to the middle tier and the third tier, so that users can access data in the DW and also directly from data sources with instant data conversion through the Internet. Semantic conflicts among various data sources exist and they are solved in the middle tier.

DW is designed with a multidimensional database. A multidimensional database is required to overcome limitations of the traditional relational database management systems (RDBMS). Multidimensional databases are based on RDBMS, but they easily perform elaborate and complex queries by being coupled with On-Line Analytical Processing (OLAP). The three-tier architecture also includes wrappers to extract information from various data sources. The wrappers stay in the middle tier and are mainly responsible for data and schema conversion to help users access data directly in data sources. Metadata management is performed in data warehouse and includes data mapping, conversion, and summarization to store data in the data warehouse.

Data volumes will continuously grow and the data warehouse size will also rapidly grow. Multiple servers are required to implement a data warehouse with fast growing data volumes. Based on data usage patterns, data distribution is also necessary. To extract data from various data sources, a wrapper for each data source should be implemented. Each wrapper will semi-automatically extract data from a data source and a module in the middle tier loads, cleans, transforms, and migrates the extracted data into data warehouse. To implement the data warehouse, both a relational database management system and an on-line analytical process tools are required. The middle tier has data mining modules to discover knowledge from data collected from various sources and data in the data warehouse in real time mode. Data mining is also performed in batch mode for non time-sensitive applications.

The goal of data mining is to discover knowledge such as hidden relationships, patterns, or correlations from a collection of data. The DW will have a massive amount of data. It is hard to investigate manually the data in DW due to the excessive amount of data. Data mining can be used to perform clustering, classification, find associations and correlations. Data mining can give results in real-time, and provide strategic value in time-sensitive situations.

Hypothesis and Evaluation. Our hypothesis is that the proposed three-tier architecture for the DW will facilitate data organization and data access via Internet for geographically

distributed users. It will also provide seamless data interoperability among various data sources by providing ways to resolve semantic conflicts. The data mining module will provide knowledge that is hidden in massive amounts of data. We will evaluate our architecture by providing multidimensional conceptual view, transparency, accessibility, flexible reporting, multi-user support, and knowledge discovery by data mining and measuring user satisfaction. We will also evaluate our system based on response time by measuring the time taken between user queries and the results. We can also evaluate the knowledge discovered by data mining techniques by showing them to domain experts.

1.2.2 Expected Results or Benefits: TKM

As goals one and two are attained, we will have the CAMRA community of members in the domain of microbial risk assessment (MRA) team that are familiar with submitting, retrieving, and reusing the proposed knowledge repository. CAMRA members will have benefited from its knowledge sharing and leveraging capabilities and the technological support for collaborative learning. The learning unit will have a stable representation specification, which is suitable to the domain and its users. A hierarchical task network will represent the main tasks and processes in the domain and how they interrelate and will be used to facilitate knowledge storing, retrieval, and reuse. The understanding of the field of MRA will have been enhanced. Learning units in the knowledge repository will embed the necessary understanding to create solutions to problems associated with MRA, such as environmental and public heath.

As our third goal is achieved, all the communities involved with MRA will have online access to a complex database. Users can discover knowledge in real time and generate flexible reports and summary of a set of data from the data warehouse. The knowledge in the field will be expanded further through data mining algorithms uncovering MRA knowledge. The extension of its value can be only imagined as every citizen in the world with Internet access and understanding of the English language will be able to learn about environmental problems, improving the public's ability to protect the environment and human health..

1.3 Communication Knowledge Management, Transfer, and Learning (CKM) to the Public

Enhanced concern over the need for protection of water, food and the environment from terrorist agents of a microbial nature has prompted an urgent need for experts to cope with such contamination and to determine their potential risks to the U.S. population. Currently, the U.S. is faced with a lack of expertise in microbiological risk assessment (MRA) for agents transmitted by food, water and air, both from natural and deliberate sources, and there are few academic programs targeted to address this shortage. In addition there is no established framework in which the community of users of assessments could apply the current sets of data, tools and models.

CAMRA will be dedicated to providing meaningful and active communication and learning experiences for those in biosecurity. This will be addressed through collaboration with other DHS centers for example (post-harvest food protection and defense and foreign animal diseases) and creation of linkages with other successful, but presently independent, programs delivered by universities, associations and private contractors.

1.3.1 Approach to CKM

Goal 1: To develop an intellectual knowledge base

An intellectual knowledge base will be formed, that public entities will have access to. This will address the integration of fields of security, water and food supply, environment and public health, with a special focus on microbial risk assessment and select agents. The initial database will be strong on the water/food supply chain models and it will take longer to build up the information on the select agents. This nucleus of intellectual resources will be initiated within the consortium but eventually will create a nationwide learning community with additional expertise from other academic and government units as required to respond to the meet EPA and DHS objectives and the continual changing need for education for government and industry professionals. This will include representatives of the other DHS centers (Table)

Goal 2: To develop CAMRA website and other dissemination means

A CAMRA website will facilitate access to developed resources. This needs to be input by agent, means of delivery (e.g., air, water, food), current risk assessment information (e.g., dose response and exposure data), different frameworks for management approaches. This information will be shared with the learning community for evaluation, enhancement and development strategies. Other ways to engage public participants interested in application of MRA may include listservs, and bulletin boards.

Goal 3: To develop a series of CAMRA workshops

Each CAMRA member belongs to any one of a number of professional organizations that provide opportunity for communicating CAMRA research and assessments to professional colleagues in a variety of arenas. Normally pre-conference or conference workshops can be developed and submitted, thus reaching a number of different disciplines and potential impacting the community of practice by various types of professions, which could then begin to incorporate the principals of MRA. CAMRA plans to design a series of workshops that can be presented by CAMRA scientists at a variety of meetings such as: American Society of Microbiology, ASM BioDefense Research Meeting, American Public Health Association, American Water Works Association, Institute for Food Technology, Society for Risk Analysis, Water Environment Federation.

In addition, workshops can be tailored specifically toward EPA and DHLS scientists. These may be held directly at EPA research facilities or at MSU facilities.

1.3.2 Benefits of CKM

Risk assessments are not ends in themselves but are a part of risk management strategies for controlling or reducing the impact of diseases of concern. Such assessments depend on the specific questions asked by the managers. So, there has to be dialog between assessors and managers to agree on the most appropriate questions and the available information and resources to accomplish this. Risk assessments are increasingly being used to influence existing policy for a specific agency, e.g., the FDA/FSIS Listeria monocytogenes risk assessment in the U.S. (2003) or as guidance to set policy for any country, e.g., the FAO/WHO also for L. monocytogenes (2004). Thus this program will allow professionals to obtain research data, utilize that

information to assist in the development of recommendations for policy to reduce the risk of transmission of select and other agents to populations in the U.S. It is hoped that in response to an event, work with Risk Assessment and Public Health Cores to develop educational strategies to support response and recovery activities can be undertaken.

1.4 Educational Knowledge Management, Transfer, and Learning (EKM)

1.4.1 Introduction

Clearly one of the main communities CAMRA would like to reach is the graduate student population and post-doctoral research scientists that will be supported by the Center as well as any involved with the investigators at each University. CAMRA will support up to14 students as well as 6 to 10 post-doctoral scientists. These individuals will form the CAMRA educational consortium of students for the study of MRA

Mission. The Education Core will facilitate the translation of research into practice, policy and response. This will occur through the development and dissemination of education programs, the integration of best practices and cutting-edge methods into academic course materials, and the development of platforms for creating virtual training programs incorporating courses from university collaborators within and beyond the consortium.

1.4.2 Approach

Core Description. The Education Core combines some of the nation's most prominent educators in the agriculture, food science, veterinary medicine, and public health disciplines to create a team that can work across the food chain to promote microbial risk assessment.

Core Activities:

Task 1: Review research activities with project leaders and work groups to identify material that can be incorporated into just-in-time and academic training courses

Task 2: Initiate institutional processes to facilitate seamless transfer of academic course credits between institutions. Initial core locations and members: Todd [MSU], Gurian [Drexel], Pepper [U Ariz], Koopman [U Mich], Casman [Carnegie Mellon], and Nicas/ Eisenberg [UC Berkeley] Advisors: EPA DHS and other interested stakeholders.

Task 3: One semester online course: The on line version will use training modules along the lines of the MSU NFSTC Pro MS distance learning course, and cover the latest developments in risk microbial assessment through computer access and instructors via the web or online. It will allow demonstration of all the detection, modeling, and quantitative risk assessment tools, and have three layers: Layer 1 will be focused on novices and administrators; Layer 2 will target graduate students interested in getting the training so they can begin to use the knowledge to do research; and Layer 3 will be geared towards the experts or working professional planning to become experts or increase their knowledge. It will be team-taught through modules by all the Center participants and other experts. By accumulating research and educational materials from a collection of risk assessment experts throughout the world, administrators, graduate students and others would be provided with the knowledge needed to combat suspected or actual contamination events. The flexibility of the online environment allows participants to receive this information without sacrificing other commitments. Additionally, the online environment permits the inclusion of the latest news and updates in microbial risk assessment.

There are a number of other programs and approaches that will be discussed. For example the "Development Multi-day international workshops at the expert level". This program would be designed as a forum for providing and gathering the latest research, technology and developments on microbial risk assessment to generate information to be put into courses/programs, along with contacts with expert who could contribute to these. Consortium members would serve as the hosts for international gatherings of experts and guest presenters. This approach is based on the Texas A&M Food Irradiation workshop held in April 2004. One could also develop a Project-driven Graduate to Post-doc visitation program in multiple settings. This would allowing advanced students the opportunity to work side-by-side with experts in the field of microbial risk assessment, the project-driven visitation program puts students in a position to learn from the best in an active, focused manner on multiple campuses. By collaborating in research through a project-driven approach, students can participate in a semester-long program at host universities. Through collaboration with grant-funded university partners students will seek fellowships to allow them opportunities to spend several months at each of the participating institutions working with the experts to learn and develop strategies for microbial risk assessment in different scenarios, e.g., water, food, air, person to person and with different organisms

1.4.3 Expected Results or Benefits: EKM

Critical to the protection of our nation's water, food and environmental infrastructures is the development of educational resources and experts enabled to react during a potential or ongoing crisis or to plan ahead for introducing strategies to anticipate risks. By utilizing a variety of educational methods, MSU, Drexel University of Arizona and University of California Berkeley are fulfilling their role as leaders in countering terrorism and risk assessment, but these need to be combined to allow to educate the next generation of scientists on the science, methodologies and applications of MRA.

CAMRA is committed to fulfilling the EPA's and DHS's mandates to meet the need for protection and defense. Such a challenge requires evaluation and strategic planning never before undertaken. Several initiatives are required:

1. To build educational programs around existing programs such as enteric pathogens in water/food scenarios, integrating supply-chain management, economic and health assessments, detection and diagnostic needs, and public health concerns.
2. To tap disciplines such as agriculture, criminal justice, engineering, epidemiology, food science, microbiology, mathematics, public health, veterinary medicine, and water research, to increase the number and diversity of students and trainees. Recent examples of this effort are:

a. The MSU Online Professional Master of Science (proMS) in Food Safety Degree Program accepted 31 students during its first two years with a projected enrollment of 50 in 2004.
b. In September 2004, the MSU School of Criminal Justice received a $3 million grant from the DHS's Office of State and Local Government Coordination and Preparedness to help law enforcement agencies across the nation gather and manage information, and specifically to develop a program to help more than 1,100 local, state and tribal law enforcement officials as they seek to protect the public.
c. The MSU School of Criminal Justice, in collaboration with colleges across campus, has launched a three-course online certificate program that allows working professionals and

graduate and undergraduate students to add a specialization in homeland security to their career or academic plans.

d. The Michigan Department of Agriculture and the Michigan Veterinary Medical Association are all part of the Michigan Emergency Veterinary Network, or "Vet Net," an integral part of Michigan's homeland security efforts in the animal health and protection arena. Vet Net is made possible by DHS and MSU College of Veterinary Medicine funding. The program includes two main components: a general education series for all veterinarians and an in-depth emergency preparedness training program for those who sign up to serve in the "corps."

e. MSU is a part of the Minnesota-led University Center for Post-Harvest Food Protection and Defense, sharing a three-year, $15 million grant from DHS to improve agro-security, including developing bio-sensors that can detect anything from anthrax to botulism, and radio frequency identification (RFID) tags that can help track packages, as well as vulnerability assessment for supply chains, and the education program.

The base of these programs should include the general principles of microbiological risk assessment as follows:

1. Microbiological Risk Assessment should be soundly based upon science.
2. There should be a functional separation between Risk Assessment and Risk Management.
3. Microbiological Risk Assessment should be conducted according to a structured approach that includes Hazard Identification, Hazard Characterization, Exposure Assessment, and Risk Characterization.
4. A Microbiological Risk Assessment should clearly state the purpose of the exercise, including the form of Risk Estimate that will be the output.
5. The conduct of a Microbiological Risk Assessment should be transparent.
6. Any constraints that impact on the Risk Assessment such as cost, resources or time, should be identified and their possible consequences described.
7. The Risk Estimate should contain a description of uncertainty and where the uncertainty arose during the Risk Assessment process.
8. Data should be such that uncertainty in the Risk Estimate can be determined; data and data collection systems should, as far as possible, be of sufficient quality and precision that uncertainty in the Risk Estimate is minimized.
9. A Microbiological Risk Assessment should explicitly consider the dynamics of microbiological growth, survival, and death in the different environments (water, food, air) and the complexity of the interaction between human and agent following consumption in causing disease (including sequelae), as well as the potential for further spread.
10. Wherever possible, Risk Estimates should be reassessed over time by comparison with independent human illness data.
11. A Microbiological Risk Assessment may need reevaluation, as new relevant information becomes available.

CAMRA will be focused on knowledge, communication and learning that will take train the scientists of the future in MRA methods and research which will aid in further enhancing frameworks that will be useful for recommendations for policy to reduce the risk of transmission of select and other agents to populations in the U.S.

1.5 General Project Information

1.5.1 Personnel and Management :

The project will be overseen by Dr. Rosina Weber (Drexel) for all activities relating to knowledge management for CAMRA and By Dr. Ewen Todd for all knowledge management for the public and educational community groups. Each will be supported with a team but will have significant interactions with teams at each university in addition to Project teams. There will be significant discussions directly with the ESI team.
The College of Information Science & Technology at Drexel University represents a unique combination of expertise in the areas of knowledge management, computational intelligence, databases, collaborative learning, and human-computer interaction. Dr. Rosina Weber will be overseeing all aspects of the repository data base, knowledge discovery and lessons learned for the CAMRA scientists and colleagues who are specifically involved in MRA methodology. Dr. Michael Atwood's will be involved in the development of interactive systems and expert systems, software engineering process improvement, software project management, and software product development. Dr. Hyoil Han's interest will be in the merging of techniques from the areas of databases and artificial intelligence; including databases, data mining, stream data mining/management, machine learning techniques, relational learning, bioinformatics, and information extraction.

Dr. Ewen Todd will lead in the development of web sites for the public domains, oversee the educational programs and address the interactions with EPA and DHLS. In addition, He will work directly with Dr. Rose to establish the set of workshops and work via the ESI to establish a graduate level curriculum. He will be assisted with the hiring of a Post-doctoral scientist with the expertise in MRA and computational programs.

1.5.2 Facilities:

College of Information Science & Technology (IST), Drexel University
Laboratories: Computing Support for Research-dedicated facilities. IST houses two newly renovated research facilities that have substantial computing facilities. The Knowledge Management Collaboratory (KMC) contains 15 PC P3-700 workstations with flat panel monitors and connected by a mixed wired and wireless network, a SmartTech smart board rear projection unit, and an InSight controller. The KMC is supported by an IBM NetFinity dual P3-700 server with 2 gigabytes of RAM (upgradable to 10) and a maximum 360 gigabyte storage capability. A UNYSIS server with 1-2 gigabytes of RAM and 720 gigabytes maximum storage capacity is also online. This provides an excellent facility in which to study collaborative design. The Usability Laboratory contains 6 PC computers, a Panasonic front projection unit, and a mirror for observation of participants in experiments. This provides an excellent facility in which to verify the usability of systems developed in research projects. Two more laboratories are of exclusive use of graduate students. All workstations in all these labs are networked via Ethernet and utilize 2 high-end servers currently running Windows NT 4.0 Server for print and file services.
Software. The University and College hold licenses for a range of research-related software, including standard statistical packages, Web-authoring tools, and various graphics software. Specifically for this project, we will build the knowledge repository using PHP and MySQL,

which are free and extremely reliable. For the data warehouse, we must purchase a license of Oracle so we can use its data warehousing capabilities to be efficient and less prone to error.
Computer. Computing services in IST support general college administrative and service functions, classroom instruction and student work, and faculty teaching and research. This PI has one workstation located in her office, one laptop for her use, and one laptop being used by her and students working under her supervision. These are the respective configurations.
1). Dell Optiplex GX150 includes: PIII 1Ghz processor, 256K cache, PCIRiser 512MB PC133 SDRAMM (2@256MB DIMMS); 19" viewable monitor; 32MB nVidia AGP:40GB 7200RPM ATA hard drive. 2.) IBM T41p laptop includes: 2373GEU IBM ThinkPad T41p 2373-Pentium M 1.7 GHz: wireless LAN antenna, Cache Memory 1 MB-L2 cache:RAM 512 MB (installed)/2 GB (max); Ethernet, Fast Ethernet, Gigabit Ethernet, Bluetooth, IEEE 802.11b, IEEE 802.11a, IEEE 802.11g. 3). DELL Latitude L400 laptop includes:PIII 800 Mhz with 12" display:512MB SDRAM :80GB hard drive
Major equipment. The major equipments to be used in this project are the new workstation to be purchased, the computers in the KMC, and this PI's computers.
Secretarial. IST provides good secretarial support that includes work-study students. These students are allocated on a term basis.
Connectivity. The entire College building is Ethernet networked with a capacity equivalent to a T1 line, feeding off of a campus wide T3 backbone. Drexel is also a wireless campus (802-11B wireless network) with each building containing from 1 to 5 transceivers. Students and faculty have full laptop wireless access to the entire range of university services, any place, and any time. Drexel and Penn both use the new Internet2 connection to the Internet, permitting extremely fast connectivity and the rapid transfer of very large files.

MSU Facilities

The NFSTC has a 3-story 115,000-sq. ft. building with laboratories for researchers with expertise in toxicology, carcinogenesis, pathology, analytical chemistry, microbiology, epidemiology and the social sciences. It is also the location of outreach and education programs, seminars and workshops. It is also the home of the newly created Food Safety Policy Center. Thus, this is a suitable building to conduct seminars and workshops relating to risk assessment and how these can interact with research and policy. As seminar room with room for up to 40 participants with computers is available for these. Courses/workshops conducted there will be modified for taking to other locations and involving other consortium members. The post-doc with expertise in MRA, will develop courses along with the experts from the other consortia under the direction of Dr. Todd. Dr. Todd will also coordinate the MRA educational activities with those arising out of the DHS NCFPD coordinated by Dr. Ed Mather who is Deputy Director of the NFSTC.

1.5.3 Time frame

Table V-1. Planned activities

KNOWLEDGE BASE AND LEARNING FOR CAMRA	Year 1	Year 2	Year 3	Year 4	Year 5
Setup and Hiring	|||||||||				
Designing Knowledge Repository	|||||||||				
Implementing Knowledge Repository	|||||||||				
Visits to Community Members	|||||||||				
Studying Learning Units	|||||||||	|||||||||			
Maintenance of Knowledge Repository- Building HTN	|||||||||	|||||||||			
Applying Reasoning Methods on the Knowledge Repository		|||||||||			
Designing and Implementing Data Warehouse			|||||||||		
Designing Learning Methods for the DW			|||||||||	|||||||||||	
Implementing Learning Methods for the DW				|||||||||||	
Review Meetings- CAMRA Meetings	|||||||||	|||||||||	|||||||||	|||||||||||	|||||||||
Workshop					|||||||||
KNOWLEDGE BASE FOR EXTERNAL PUBLIC AND EDUCATIONAL DOMAINS	Year 1	Year 2	Year 3	Year 4	Year 5
Set up and formation of educational core and web sites	|||||||||				
Initiation of workshop bringing in experts	|||||||||				
Holding of workshop, initiates contacts with other DHS centers		|||||||||			
First trial of on-line course with instructors in place selecting one of the three layers (Layer 1)		|||||||||			
Education core revises the on-line course for layer 1 and add beta versions of Layers 2 and 3		|||||||||			
Explore Student fellowships allow in-depth studies at all the CAMRA institutions		|||||||||			
Expansion of the on-line course with data generated from the exposure and dose response assessment research and from other academic institutions			|||||||||		
Continuation of on-line course, expert workshops and student fellowships in Years 4 and 5 to become both national and international			|||||||||	|||||||||	|||||||||
Courses self-sufficient			|||||||||	|||||||||	|||||||||
Professional workshops at national meetings		|||||||||	|||||||||	|||||||||	|||||||||

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BIOGRAPHICAL SKETCH	
NAME **Joan Bray Rose**	POSITION TITLE **Homer Nowlin Chair in Water Research**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Arizona; Tucson, AZ	B.S.	1976	Microbiology
University of Wyoming; Laramie, WY	M.S.	1980	Microbiology
University of Arizona; Tucson, AZ	Ph.D.	1985	Microbiology

Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Positions

1989 - 1994: Assistant Professor, College of Public Health, University of South Florida
1995-1998: Associate Professor, College of Marine Science, University of South Florida
1998 – 2002: Professor, College of Marine Science, University of South Florida
2003-present: Homer Nowlin Endowed Chair for Water Research, Michigan State University

Honors

Appointed to Michigan Environmental Science Board for the Governor of Michigan, Feb.20,(04)
Appointed to the Science Advisory Board of the Environmental Protection Agency, Drinking Water Committee, 2004-07; Chair 2004-07
Appointed to the Science Advisory Board of the International Joint Commission of the Great Lakes, 2003-05
Elected to the Research Advisory Council for the Water Reuse Foundation, 2003-06.
Elected Vice Chair : USA National Committee for the International Water Association, 2002-05
Elected Chair of the International Water Association's Specialty Group "Health-Related Water Microbiology" 2003-2007
Appointed to the Research Advisory Board, National Water Research Institute, 2002-04
Elected to the Board of Directors, Association of Environmental Engineering and Science Professors, 2002-04
Elected to the Council Policy Committee for the American Society of Microbiology, 2001-2004
Received the Athalie Richardson Irvine Clarke Water Prize. Presented July 2001 at Costa Mesa, CA. for significant contributions to Water Science and Technology, from the National Water Research Institute.
Appointed to Life Sciences Board of National Academy of Science, National Research Council, 2001-2004.
Appointed to Water Science and Technology Board of National Academy of Science, National Research Council, 1998-2004, Vice Chair.

Selected peer-reviewed publications (in chronological order) of 250

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Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Joan B. Rose	Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Occurrence and removal of Blue Green Algae and their toxins by water treatment

Source of Support: American Water Works Association Research Foundation

Total Award Amount: $100,133 Total Award Period Covered: 2/01/03-12/31/04

Location of Project: Michigan and Florida

Person-Months Per Year Committed to the Project. 1.2 Cal: x Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Microbiological Monitoring for Central Florida Artificial Recharge Demonstration Program

Source of Support: CH2MHILL Engineering

Total Award Amount: $55,750 Total Award Period Covered: 4/15/03-12/30/04

Location of Project: Michigan and Florida

Person-Months Per Year Committed to the Project. .5 Cal: x Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Microbial Risk Assessment In Drinking Water Development of a Biochip Development Of A Virulence Factor Biochip And Its Validation

Source of Support: EPA

Total Award Amount: $600,000 Total Award Period Covered: 1/05-12/08

Location of Project: MSU

Person-Months Per Year Committed to the Project. 1.2 Cal: x Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Microbiological Research Unit for Waterborne and Foodborne Disease

Source of Support: National Institute of Health

Total Award Amount: $400,000 Total Award Period Covered: 10/03-9/08

Location of Project: MSU

Person-Months Per Year Committed to the Project. 1.2 Cal: X Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Center of Excellence for Great Lakes and Human Health

Source of Support: NOAA

Total Award Amount: $1,500,000 Total Award Period Covered: 9/04-8/09

Location of Project: MSU

Person-Months Per Year Committed to the Project. .6 Cal: X Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

(See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Joan B. Rose

Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Influence of Combined Sewer Overflows on Cryptosporidium and Giardia in Sediments and Impacts on Water Quality and Health in the Great Lakes

Source of Support: NOAA

Total Award Amount: $600,000 Total Award Period Covered: 10/15/04-10/14/07

Location of Project: Michigan

Person-Months Per Year Committed to the Project. 0.5 Cal: X Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Water Quality of Three Impaired Southern Michigan Rivers Discharged in the Great Lakes

Source of Support: Michigan Sea Grant

Total Award Amount: $ 200,000 Total Award Period Covered: 12/01/04-2/28/06

Location of Project: MSU

Person-Months Per Year Committed to the Project. 0.25 Cal: X Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Genosenoser for Detection of Viruses in Coastal Waters

Source of Support: National Science Foundation
Total Award Amount: $ 1.2 mil Total Award Period Covered: 7/01/03-6/30/07
Location of Project: University of South Florida and MSU
Person-Months Per Year Committed to the Project. 1.2 Cal: x Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Epidemiology of Groundwater and Waterborne disease

Source of Support: Environmental Protection Agency
Total Award Amount: $ 158,000 Total Award Period Covered: 9/01/03-8/30/06
Location of Project: Emory University and Hillsborough County
Person-Months Per Year Committed to the Project. 0.5 Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NSF Form 1239 (10/98) USE ADDITIONAL SHEETS AS NECESSARY

Curriculum Vita of Charles N. Haas

Professional Preparation.

B.S. (Biology), Illinois Institute of Technology, 1973.

M.S. (Environmental Engineering), Illinois Institute of Technology, 1974.

Ph.D. (Environmental Engineering in the Department of Civil Engineering), University of Illinois, Urbana, Illinois, 1978.

Appointments

2003– Interim Head, Department of Civil, Architectural and Environmental Engineering, Drexel University (18 faculty, 4 staff, 500 students).

2003--: Research Professor, Department of Emergency Medicine, Drexel University College of Medicine

1991– :Betz Chair Professor of Environmental Engineering, Drexel University.

1989-1990: Acting Chairman, Pritzker Department of Environmental Engineering, Illinois Institute of Technology

1988-1989: Visiting Professor of Environmental Engineering, University of Illinois at Urbana-Champaign

1981-1990: Assistant Professor (1981-83), Associate Professor (1983-87), Professor (1987-90) Illinois Institute of Technology

1978-1981: Assistant Professor of Environmental Engineering in the Department of Chemical and Environmental Engineering, (1979-1981), Acting Director of Environmental Engineering Programs, Rensselaer Polytechnic Institute

Honors and Awards

American Academy of Microbiology, Elected as Fellow (1997)

Society for Risk Analysis, Fellow (2002)

American Association for Advancement of Sciences, Fellow (2003)

Univ. of Illinois at Urbana Champaign, Dept. of Civil & Envtl. Eng., Distinguished Alumnus Award (2003)

Harvey Rosen Award, International Ozone Association (2003)

Publications Most Closely Related to the Proposed Work

Quantitative Microbial Risk Assessment, C.N. Haas, J.B. Rose and C.P. Gerba, John Wiley (NY) (1999).

“Importance of Distributional Form in Characterizing Inputs to Monte Carlo Risk Assessments”, CN Haas, Risk Analysis, 17(1):107-113 (1997).

"Managing Health Risks from Drinking Water -- A Report to the Walkerton Inquiry", Journal of Toxicology and Environmental Health -- Part A, 65:1635-1823 (2002). D. Krewski, J. Balbus, D. Butler-Jones, C. Haas, J. Isaac-Renton, K.J. Roberts, and M. Sinclair.

"The Role of Risk Analysis in Understanding Bioterrorism", C.N. Haas, Risk Analysis, 22(4):671-7 (2002).

“On the Risk of Mortality to Primates Exposed to Anthrax Spores”, C.N. Haas, Risk Analysis, 22(2):189-93 (2002).

"Risk Assessment of Waterborne Coxsackievirus", K.D. Mena, C.P. Gerba, C.N. Haas and J.B. Rose, Journal of the American Water Works Association, 95(7):122-131 (2003).

Key Professional Activities

Member, Panel on Augmentation of Potable Water Supplies with Reclaimed Water, National Academy of Sciences, Water Science and Technology Board, 1996-1998.

Member, Committee to Review New York City Watershed Management Strategy, National Academy of Science, Water Science and Technology Board, 1998-99.

Member, Committee on Drinking Water Contaminants, National Research Council Water Science and Technology Board, 1999-2001.

Member, Panel to Review EPA Research Plan on Water Security, National Research Council, Water Science and Technology Board, 2003-.

Member, Committee on Standards and Policies for Decontaminating Public Facilities Affected by Exposure to Harmful Biological Agents: How Clean is Safe? National Research Council, Board on Life Sciences, 2003-current.

Member, Water Science and Technology Board, National Academies, 2004-current.

Member, Water Environment Federation House of Delegates, 2004-current.

Related Prior and Current Research

Co-Principal Investigator, "Microbial Risk Assessment", American Water Works Association Research Foundation (1993-1995, $90,000).

Principal Investigator, "Risk Assessment from Sewage Discharges in Mamala Bay, HI", (Mamala Bay Commission), 1995, $35,000.

Principal Investigator, "Risk Assessment of Heterotrophic Organisms in Point of Use Devices", (Water Quality Association), 1995-1996, $15,000.

Co-Principal Investigator, "Extension of Quantitative Microbial Risk Assessment Methods to Foodborne Pathogens", International Life Sciences Institute, 1997-1998, $85,000 .

Co-Investigator, "Protocol for *Cryptosporidium* Risk Communication to Drinking Water Utilities", AWWA Research Foundation, 1998-1999.

Principal Investigator, "Use of Microbial Risk Modeling to Determine the Benefits of Topical Antimicrobial Products", Soap and Detergent Association, 2000-2002, $163,000.

Principal Investigator, "Building Biodecontamination: A Process Engineering Approach", National Science Foundation, 2003-current, $99,500.

Principal Investigator, "Assessment of Physical Scale Models for Development of Room Decontamination Design Criteria", funded via National Bioterrorism Civilian Medical Response Center (CIMERC), 2004-5, $55,000.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this

Investigator: Charles N Haas	Other agencies (including NSF) to which this

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Building Biodecontamination: A Process Engineering Approach

Source of Support: NSF
Total Award Amount: $99,800 Total Award Period Covered: 10/03-9/05
Location of Project: Drexel University
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.24

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Workshop on Advancing the Quality of Water (AQWA)

Source of Support: NSF
Total Award Amount: $99,000 Total Award Period Covered: 11/03-4/05
Location of Project: Drexel University
Person-Months Per Year Committed to the Project. 0.1 Cal: Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Development of Standard Procedures for Microbial Source Tracking

Source of Support: Philadelphia Water Dept
Total Award Amount: $$23,000 Total Award Period Covered: 7/04-6/05
Location of Project: Drexel University
Person-Months Per Year Committed to the Project. Cal: 0.1 Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE/INSTITUTION
Carole Ann Bolin, DVM, PhD	Professor Dept. of Pathobiology and Diagnostic Investigation College of Veterinary Medicine Michigan State University

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Purdue University, West Lafayette, IN	BS	1978	Animal Science
Purdue University, West Lafayette, IN	DVM	1982	Veterinary Medicine
Iowa State University, Ames, IA	MS	1984	Veterinary Pathology
Iowa State University, Ames, IA	PhD	1986	Veterinary Pathology

Project/Proposal Title:

Development of Design Alternatives for Wastewater Disinfection in Chicago

Source of Support: CTE Engineers (from Metro Water Reclam Dist of Chicago)

Total Award Amount: $50,000(est) Total Award Period Covered:

Location of Project: Drexel University

Person-Months Per Year Committed to the Project. Cal: 1 Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Transport and Microbial Inactivation in a Counterflow Ozone-Water Flow

Source of Support: NSF

Total Award Amount: $485,000 Total Award Period Covered: 4/05-3/08

Location of Project: Drexel University

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

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Research and Professional Experience:

1982-1984 Postdoctoral Research Associate, Veterinary Pathology, USDA/ARS/National Animal Disease Center, and Iowa State University, College of Veterinary Medicine, Ames, IA

1984-1987 Veterinary Medical Officer, Lead Scientist, Avian Colibacillosis Research Project, USDA/ARS/National Animal Disease Center, Ames, IA

1987-1990 Supervisor Veterinary Medical Officer, Lead Scientist, Leptospirosis and Mycobacteriosis Research Projects, USDA/ARS/National Animal Disease Center, Ames, IA

1990-1995 Research Leader, Leptospirosis/Mycobacteriosis Research Unit, USDA/ARS/National Animal Disease Center, Ames, IA

1995-2000 Research Leader, Zoonotic Diseases Research Unit, USDA/ARS/National Animal Disease Center, Ames, IA

2000-Present Professor, Department of Pathobiology and Diagnostic Investigation and Section Chief of Bacteriology/Mycology, Diagnostic Center for Population and Animal Health, College of Veterinary Medicine, MSU, East Lansing, MI

Awards and Other Professional Activities: Grant Review Panels: NIH/NIAID Panel Member: 1994; IFAFS Joint USDA/NSF Genomics Grants: 2001, 2002; NIH, NIAID panel on Anthrax Vaccines: 2003, 2004;Co-Chair, USDA Workshop for Prioritization of Animal Pathogens for Genomic Analysis, 02;Editor, Journal of Clinical Microbiology, 1999-present

WHO Workshop on Waterborne Zoonoses—panel member and author of 3 monograph chapters

Honors C. L. Davis Foundation Veterinary Pathology Scholarship Award, 1986; Daniel E. Salmon Award-Outstanding Federal Veterinarian, Nat Assn. Federal Veterinarians, 1990; USDA, ARS, Performance and Special Act Awards, 1986-1995;USDA, Secretary of Agriculture's Honor Award, 1999; OIE Designated Expert on Leptospirosis, 1992-2000.

Publications (last 3 years):

Matsunaga, J., T. A. Young, J. K. Barnett, D. Barnett, C. A. Bolin, and D. A. Haake 2002. Novel 45-Kilodalton Leptospiral Protein That Is Processed to a 31-Kilodalton Growth-Phase-Regulated Peripheral Membrane Protein Infect Immun. **70:**323-334.

Morgan J, Bornstein SL, Karpati AM, Bruce M, Woods CW, Lingappa J, Austin CC, Davis B, Ashford DA, Bolin CA, Bajani M, Bragg S, Shutt K, Tappero JW, and the Leptospirosis Working Group. 2002. Leptospirosis outbreak among triathlon participants and community residents of Springfield, Illinois, 1998. *Clin. Inf. Dis*. 34(12):1593-1599.

Erskine R, Walker RD, Bolin CA, Bartlett PC, and White DG. Trends in Antibacterial Susceptibility of Mastitis Pathogens During a Seven Year Period. *J. Dairy Sci.* 85(5):1111-1118.

Wild CJ, Greenlee JJ, Bolin CA, Barnett JK, Haake DA, and Cheville NF. 2002. An improved immunhistochemical diagnostic technique for technique for canine leptospirosis using antileptospiral antibodies on renal tissue. *J. Vet. Diagn. Invest.* 14:20-24.

Naiman BM, Blumerman S, Alt DP, Bolin CA, Brown R, Zuerner R, and Baldwin CL. 2002. Evaluation of type 1 immune response in naïve and vaccinated animals following challenge with *Leptospira borgpetersenii* serovar Hardjo: involvement of WC1(+) gammadelta and CD4 T cells. *Infect. Immun.* 70(11):6147-6157.

Brown RA, Blumerman S, Gay C, Bolin CA, Duby R, and Baldwin CL. 2003. Comparison of type 1 immune responses to *Leptospira borgpetersenii* serovar hardjo induced by three different leptospiral vaccines. Vaccine 21:4448-4458.

Zhao S, Qaiyumi S, Friedman S, Singh R, Foley SL, White DG, McDermott PF, Donkar T, Bolin C, Munro S, Baron EJ, and Walker RD. 2003. Characterization of *Salmonella enterica* serotype Newport isolated from humans and food animals. J. Clin Microbiol. 41:5366-5371.

Matsunaga J, Barocchi MA, Croda J, Young TA, Sanchez Y, Siqueira I, Bolin CA, Reis MG, Riley LW, Haake DA, and Ko AI. 2003. Pathogenic leptospira species express surface-exposed proteins belonging to the bacterial immunoglobulin superfamily. Mol. Microbiol. 49:929-945.

Bolin C, Brown C, and Rose J. 2004. Emerging zoonoses and water. (chapter) WHO Monograph on Waterborne Zoonoses.

Bolin C, Brown C, and Rose J. 2004. Leptospirosis and Some Other Waterborne Zoonoses. (chapter) WHO Monograph on Waterborne Zoonoses.

Gannon V, Bolin C, Moe C, and Reilly W. 2004. Emerging Pathogens and Emerging Patterns of Infection in Waterborne Zoonoses. (chapter) WHO Monograph on Waterborne Zoonoses.

Greenlee J, Bolin CA, Alt DP, Cheville NF, and Andreasen C. 2004. Clinical and pathologic comparison of acute canine leptospirosis caused by two strains of *Leptospira kirschneri* serovar Grippotyphosa. Am. J. Vet. Res. Accepted for publication, Jan 2004.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Carole A. Bolin	Other agencies (including NSF) to which this proposal has been/will be submitted: NA

Support: [X] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title: Validation of reference vaccines for leptopsirosis

Source of Support: USDA, APHIS
Total Award Amount: $ 724,000 Total Award Period Covered: 10/16/2003 to 9/30/2005
Location of Project: Michigan State University
Person-Months Per Year Committed to the Project. 15% time Cal: Acad: Sumr:

Support: [X] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title: Microbiology Research Unit/ Food and Waterborne Disease Integrated Research Network

Source of Support: NIH
Total Award Amount: $ 10,000,000 Total Award Period Covered: 10/1/2003 to 9/30/2010
Location of Project: Michigan State University
Person-Months Per Year Committed to the Project. 5% time Cal: Acad: Sumr:

Support: [X] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title: Bovine Tuberculosis: Epidemiology, Diagnosis, and Pathogenesis

Source of Support: USDA, NRI
Total Award Amount: $ 300,000 Total Award Period Covered: 4/01/2002 to 3/30/2005
Location of Project: Michigan State University
Person-Months Per Year Committed to the Project. 5% time Cal: Acad: Sumr:

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title: Antimicrobial Resistance in Campylobacter and Salmonella Isolated from Conventional and Organic Dairy Farms

Source of Support: USDA, NRICGP
Total Award Amount: $ 600,000 Total Award Period Covered: 10/01/2002 to 9/30/2005
Location of Project: Michigan State University
Person-Months Per Year Committed to the Project. 5% time Cal: Acad: Sumr:

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title: Bioterrorism Laboratory Response Network--Confirmatory Laboratory Level (Formerly Level "B")

Source of Support: Michigan Dept. of Community Health and CDC
Total Award Amount: $ 131,000 each year Total Award Period Covered: 10/1/04 to 9/30/2005 (renewed yearly)
Location of Project: Michigan State University
Person-Months Per Year Committed to the Project. 5% time Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

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USE ADDITIONAL SHEETS AS NECESSARY

Elizabeth A. Casman

Department of Engineering & Public Policy
Carnegie Mellon University, Pittsburgh, PA 15213
http://www.epp.cmu.edu/people/bios/casman.html
email:casman@Andrew.cmu.edu

tel: (412) 268-3756
fax: (412) 268-3757

Current Appointment

9/1997- Research Engineer (Research Faculty), Department of Engineering & Public Policy, Carnegie Mellon University

Education

9/1979-6/1985 Ph.D. The Johns Hopkins University. Geography & Environmental Engineering

9/1975-6/1977 M. S. Northern Arizona University. Microbiology

9/1967-6/1971 B. S. Syracuse University. Microbiology/Chemistry

Interests

Elizabeth Casman's research concerns the interactions between social, environmental, institutional, and technical factors in human disease, both in the contexts of the epidemiology of diseases linked to climate change and of bioterrorism surveillance and response. She is also interested in water resource issues (including water quality, quantity, and drinking water security) and regulatory policy for genetically modified organisms. Since coming to Carnegie Mellon, she has specialized in integrated assessment models of infectious disease epidemiology, building numerical models that incorporate social, technological, and economic variables into contagion models, and has co-edited a book on the contextual determinants of malaria. She is also interested in the meaning of mixed levels of uncertainty in complex models and has helped develop a risk analytic tool that relies on bounding analysis. The main focus of her bioterrorism work is the early detection of covert attacks, particularly in regards to technological limitations, and more recently, preparedness and risk communication.

Recent Publications

Elizabeth A. Casman (2004) "The Potential of Next-Generation Microbiological Diagnostics to Improve Bioterrorism Detection Speed" *Risk Analysis*, 24(3):521-536.

Ha-Duong, Minh, Elizabeth A. Casman, and M. Granger Morgan (2004) "A Strategy for Bounding Attributable Risk: a Lung Cancer Example, " *Risk Analysis*, 24(5):1071-83.

Li-Chiou Chen, Boris Kaminsky, Tiffany Tummino, Kathleen M. Carley, Elizabeth Casman, Douglas Fridsma, Alex Yahja (2004) "Aligning Simulation Models of Smallpox Outbreaks"

Proceedings of the 2nd Symposium on Intelligence and Security Informatics: ISI-2004, June 10-11, 2004, Tucson Arizona, Springer-Verlag Lecture Notes in Computer Science (LNCS).

Kathleen M. Carley, Douglas Fridsma, Elizabeth Casman, Neal Altman, Li-Chiou Chen, Boris Kaminsky, Démian Nave, and Alex Yahja (2004) "A Model of Biological Attacks on a Realistic Population," International Conference on Complex Systems, (ICCS2004) May 16-21, 2004, Boston, MA.

Martin Krayer von Krauss, Mitchell J. Small, Elizabeth A. Casman (2004) "Elicitation of expert judgments of uncertainty in the risk assessment of herbicide tolerant oilseed crops," *Risk Analysis*, accepted for publication.

F. Wu, D. Miller and E. Casman (2004) "Bt corn and Mycotoxin Reduction: Economic Impacts in the United States and the Developing World." *Journal of Toxicology – Toxin Reviews,* Aflatoxin and Food Safety Part II, **23**(2/3), pp.397-424.

Carley, K.M., Fridsma, D., **Casman, E**., Altman, N., Chang, J., Kaminski, B., Nave, D., & Yahja, A. (2003). "BioWar: Scalable Multi-Agent Social and Epidemiological Simulation of Bioterrorism Events." *NAACSOS Conference Proceedings,* Pittsburgh, PA. http://www.casos.ece.cmu.edu/projects/BioWar/carley_et_al_2003_biowar.pdf

Scott Farrow, Benoit Morel, Felicia Wu and Elizabeth Casman (2003) "Pesticide Resistance, the Precautionary Principle, and the Regulation of Bt Corn: Real and Rational Option Approaches to Decision-Making" *In*, Battling Resistance to Antibiotics and Pesticides, R. Laxminarayan, ed., RFF Press, Washington, D.C.

Elizabeth Casman and Hadi Dowlatabadi, eds., (2002) *The Contextual Determinants of Malaria*, ***Chapters:*** E. Casman, "Malaria Risk versus Malaria Potential;" B. Fischhoff, I. Fischhoff, E. Casman, H. Dowlatabadi, "Integrated Assessment of Malaria Risk;" E. Casman *et al.*, "The importance of context in defining malaria risk," Resources for the Future Press, Washington, D.C.

Elizabeth Casman, Baruch Fischhoff, Mitchell Small, Hadi Dowlatabadi, Joan Rose, and M. Granger Morgan (2001) "Climate Change and Cryptosporidiosis" *Climatic Change,* 50(1/2):219-249.

Elizabeth A. Casman, Baruch Fischhoff, Claire Palmgren, Mitchell J. Small, and Felicia Wu (2000) "An Integrated Risk Model of a Drinking-Waterborne Cryptosporidiosis Outbreak" *Risk Analysis*, 20(4):495-511.

Elizabeth A. Casman, M. Granger Morgan, and Hadi Dowlatabadi (1999) "Mixed Levels of Uncertainty in Complex Policy Models" *Risk Analysis* 19(1):33-42.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Elizabeth Casman	Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: CARA

Source of Support: : Penn State & EPA Prime

Award Amount (or Annual Rate): $300,000 Period Covered: 8/1/02 – 12/31/05

Location of Project: CMU

Person-Months Committed to the Project: Cal: .80 Acad: Summ:

Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: The Use of Bounding Analysis in Risk Analysis

Source of Support: NSF

Award Amount (or Annual Rate): $271,792 Period Covered: 9/1/02-8/31/04

Location of Project: CMU

Person-Months Committed to the Project: Cal: 3.5 Acad Summ

Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Managing The Risks of Terror & Weapons of Mass Destruction

Source of Support: McArthur Foundation

Award Amount (or Annual Rate): $1,158,000 Period Covered: 1/1/03-12/31/05

Location of Project: CMU

Person-Months Committed to the Project: Cal: 2.2 Acad: Summ:

Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Integrating Risk Analysis and Risk Communication

Source of Support: EPA

Award Amount (or Annual Rate): $749,729 Period Covered: 9/1/04-8/31/07

Location of Project: CMU

Person-Months Committed to the Project: Cal: .6 Acad: Summ:

Support: ☐ Current ■ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Enhancing The Fidelity, Performance and Analysis of Large Scale Multi-Agent Simulation Model Complex Organizational Reasoning Systems

Source of Support: NSF

Award Amount (or Annual Rate):$3,036,792 Period Covered: 8/1/04-8/1/08

Location of Project: CMU

Person-Months Committed to the Project: Cal: 2.5 Acad: Summ:

☐ Support: Current ■ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support Project/Proposal Title: The Role of Extreme Weather in Occupational Injuries Source of Support: University of Pittsburgh (NIH) Award Amount (or Annual Rate): $60,099 Period Covered: 7/1/05 – 6/30/08 Location of Project: CMU Person-Months Committed to the Project: Cal: Acad: 10% Summ:
☐ Support: Current ■ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support Project/Proposal Title: Source of Support: Award Amount (or Annual Rate) Period Covered: Location of Project: CMU Person-Months Committed to the Project: Cal: Acad: Summ:

CHRISTOPHER Y. CHOI

DEPARTMENT OF AGRICULTURAL AND BIOSYSTEMS ENGINEERING
Shantz Bldg. No 38, Room 403, The Univ. of Arizona, Tucson, Arizona 85721
Ph. (520) 621-1890 Fax (520) 621-3963 Email: cchoi@ag.arizona.edu

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Dr. Choi's research has been focused on both applied and basic engineering areas. He has placed a primary emphasis on fundamentals in transport phenomena and 'real world' applications in Agricultural and Biosystems Engineering. Upon joining the department, he sought research projects in the areas of transport phenomena in agricultural and environmental fields. In addition, he has developed research projects related to the application of modern computer technologies based on his previous experience in supercomputing and computational modeling. He has successfully established interdisciplinary research projects funded by private industries, state agencies, and federal organizations. Dr. Choi's current research interests include (i) Environmental effects on the fate of emerging pathogens in irrigation water and biosolids, (ii) Dispersion of biological agents in water systems, (iii) Numerical simulation of the transport phenomena, and (vi) Application of Internet and wireless data acquisition systems.

Chronology of Employment

7/00-Present	Associate Professor Department of Agricultural and Biosystems Engineering The University of Arizona, Tucson, Arizona
12/02-Present	Faculty, Graduate Interdisciplinary Program Department of Biomedical Engineering The University of Arizona, Tucson, Arizona
7/94-6/00	Assistant Professor Department of Agricultural and Biosystems Engineering The University of Arizona, Tucson, Arizona
7/90-6/94	Instructor and Postdoctoral Research Associate Department of Aerospace and Mechanical Engineering The University of Arizona, Tucson, Arizona

Chronology of Education

Ph.D. in Mechanical Engineering (1/87 - 6/90)

Colorado State University, Fort Collins, CO 80523

Research Area: Experimental and Computational Heat and Mass Transfer

Military Service in Korea, Honorably Discharged as 2nd Lieutenant (85-86)

M.S. in Engineering Science and Mechanics (8/83 - 6/85)

The University of Tennessee, Knoxville, TN 37996

Research Area: Computational Fluid Flow and Radiative Heat Transfer

B.S. in Mechanical Engineering (3/79 - 2/83)

Ajou University, Suwon, Korea

Patent

Ground Based Remote Sensing System (UAZ001) – Haberland, Defer, Waller, Choi, Colaizzi, Kostrevski (2000)

Refereed Journal Publications (Last Two Years)

- Choi, C. Y., I. Song, S. W. Stine, J. Pimentel, C. P. Gerba, 2004, Role of Irrigation Methods on Effluent Quality and Viral Contamination for Lettuce Production, Journal of Water Science and Technology. 50:2 61–68

- Choi, C. Y. and E. Suarez-Rey, 2004, Subsurface Drip Irrigation for Bermudagrass with Reclaimed Water, *Transactions of the ASAE*. 47:6 1-9.
- Enriquez, C., A. Alum, Suarez-Rey, E., Suarez-Rey, E., C. Y. Choi, G. Oron, C. P. Gerba. 2003. Survival of bacteriophages MS-2 and PRD-1 in turfgrass irrigated by subsurface drip irrigation, *American Society of Civil Engineers (ASCE) Journal of Environmental Engineers*. 129:9, 852-857.
- Colaizzi, P. D., E. M. Barnes, T. R. Clarke, C. Y. Choi, and P. M. Waller. 2003. Estimating soil moisture under low–frequency surface irrigation using the CWSI. ASCE J. Irrigation and Drainage Eng, Vol. 129, No. 1, pp. 27-35.
- Colaizzi, P. D., E. M. Barnes, T. R. Clarke, C. Y. Choi, and P. M. Waller. 2003. Water Stress Detection under High Frequency Sprinkler Irrigation using WDI. ASCE J. Irrigation and Drainage Eng, Vol. 129, No. 1, pp. 36-43.
- Kostrzewski, M., P. Waller, P. Guertin, J. Haberland, P. Colaizzi, E. Barnes, T. Thompson, T. Clarke, E. Riley, and C. Choi. 2003. Detection of water and nitrogen stress variability with the AgIIS remote sensing system. Transactions of the ASAE. 46(1): 29-38.

Other Relevant Publication

- Choi, C. Y., C. P. Gerba, and M. Riley, 2003. Environmental Dispersion of Biological Agents in Sewer Systems. 150 page Report for the DARPA No. 806345617.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Christopher Y. Choi	Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Pathogen Reduction in Biosolids in Solar Drying Beds Prior to Land Application

Source of Support: IALC/USAID
Total Award Amount: $39,000 Total Award Period Covered: 7/1/04-8/31/05
Location of Project: University of Arizona
Person-Months Per Year Committed to the Project. Cal: 1.0 Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Pathogen Reduction in Biosolids for Land Application by Solar Drying

Source of Support: LASD
Total Award Amount: $25,000 Total Award Period Covered: 1/1/04-12/31/05
Location of Project: University of Arizona
Person-Months Per Year Committed to the Project. Cal: 0.25 Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Design and Evalation of Biosolids Land Application Machinery

Source of Support: Avra Gro Systems Inc.
Total Award Amount: $10,000 Total Award Period Covered: 10/1/04-9/30/05
Location of Project: University of Arizona
Person-Months Per Year Committed to the Project. Cal: 0.25 Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Fate of Viruses during Sluge Treatment and after Land Application

Source of Support: BARD

Total Award Amount: $179,991 Total Award Period Covered: 5/05-4/08

Location of Project: University of Arizona

Person-Months Per Year Committed to the Project. Cal: 1.0 Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Microclimate and Water Use Management in Screenhouses

Source of Support:

Total Award Amount: $100,000 Total Award Period Covered: 5/05-4/07

Location of Project: University of Arizona

Person-Months Per Year Committed to the Project. Cal: 1.0 Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Joseph N.S. Eisenberg	Adjunct Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of California, Berkeley	BS	1982	Electrical Engineering
University of California, Berkeley/San Francisco	MS	1986	Bioengineering
University of California, Berkeley	MPH	1991	Public Health
University of California, Berkeley/San Francisco	PhD	1992	Bioengineering

A. Positions and Honors..

Positions and Employment

1985 - 1988 **Research Assistant**, Molecular and Cell Biology, U.C. Berkeley, Neurophysiology Lab
1988 - 1989 **Graduate Student Instructor,** Electrical Engineering, U.C. Berkeley
1989 - 1991 **Research Assistant,** School of Public Health, U.C. Berkeley**,** Arbovirus Group
1992 - 1993 **Postdoctoral Researcher,** School of Public Health, U.C. Berkeley
1993 - 1995 **Assistant Research Bioengineer,** Mechanical Engineering, U.C. Berkeley
1994 - 1996 **Postdoctoral Fellow,** Environmental Biology, NSF
1996 - 1997 **Assistant Research Bioengineer,** School of Public Health , U.C. Berkeley
1997-present **Assistant Research Bioengineer,** Infectious disease epidemiology
1998 - 2003 **Assistant Adjunct Professor**, School of Public Health, U.C. Berkeley
2003 - present **Associate Adjunct Professor**, School of Public Health, U.C. Berkeley

Committee Work

Workshop on National Environmental Burden of Disease, Geneva, Switzerland, Nov 2002
EPA Microbiological Risk Assessment Framework Workshop, Washington DC, Aug 2002
Training on infectious disease modeling, Jiangsu Institute of Parasitic Disease. Wuxi, China, Oct 2001
Workshop on defining susceptibility in microbial risk assessment. George Washington University, Jun 2001
National estimate of waterborne disease. Center for Disease Control, Atlanta, Feb 2001
Expert consultation on a methodology for assessment of environmental burden of disease. WHO, Aug 2000
Waterborne exposure routes of microbial pathogens. USEPA, Washington DC, Jun 2000
Peer-review of Ground Water Rule Risk Assessment, USEPA, Washington DC, Jun 2000
Peer-review of ORD Contaminant Candidate List Research Strategy, USEPA, Washington DC, Jan 2000

Harmonized risk assessment for water-related microbial hazards. WHO Stockholm, Sept 1999

B. Selected peer-reviewed publications

1. Eisenberg J.N., Seto E.W., Olivieri, A.W., Spear, R.C (1996) Quantifying water pathogen risk in an epidemiological framework. Risk Analysis. 16(4):549-563.
2. Eisenberg J.N.S., Seto E.W., Colford J., Olivieri, A.W., Spear, R.C (1998) An Analysis of the Milwaukee *Cryptosporidium* outbreak based on a dynamic model of disease transmission. Epidemiology, 9(3):255- 263.
3. Eisenberg J.N.S., Priest J.W., Lammie, P.J., Colford, J.M. (2001) The serologic response to Cryptosporidium in HIV-infected persons: Implications for epidemiological research. Emerging Infectious Diseases 7(6):992-997
4. Eisenberg J.N.S., Hunter P.A., Bartrum J. (2001) A public health perspective for establishing water-related guidelines and standards *in* Water quality: Guidelines, standards and Health: Assessment of risk and risk management for water-related infectious disease. (Eds. Fewtrell, L. and Bartram, J.). IWA Publishing, London.
5. Eisenberg J.N.S., Priest J.W., Lammie, P.J., Colford, J.M. (2001) The serologic response to Cryptosporidium in HIV-infected persons: Implications for epidemiological research. Emerging Infectious Diseases 7(6):992-997
7. Eisenberg J.N.S., Brookhart M.A., Rice G., Brown M., Colford J.M. (2002) Disease transmission models for public health decision making: analysis of epidemic and endemic conditions caused by waterborne pathogens. Environmental Health Perspectives 110(8):783-790.
8. Eisenberg J.N.S., Wade T.J., Hubbard A.E., Abrams D.I., Leiser R.J., Charles S., Vu M., Saha S., Wright C.C., Levy D., Jensen P., Colford J.M. (2002) Associations between water treatment methods and diarrhea in HIV positive individuals. Epidemiology and Infection 129(2):1-9.
9. Brookhart M.A., Hubbard A.E., van der Laan M.E., Colford J.M., Eisenberg J.N.S. (2002) Statistical estimation of parameters in a disease transmission model: an analysis of a *Cryptosporidium* outbreak. Statistics in Medicine 21(23):3627-38.
10. Eisenberg J.N.S., Lewis B. L., Porco T. C., Hubbard A. H., Colford J. M. Jr. (2003) Bias due to secondary transmission when estimating attributable risks reported from intervention trials. Epidemiology 14(4):442-450.
11. Wade T.J., Pai N., Eisenberg J.N.S., Colford Jr., J.M. (2003) Do US EPA water quality guidelines for recreational waters prevent gastrointestinal illness? A systematic review and meta-analysis. Environmental Health Perspectives, 111(8):1102-1109.
12. Soller J.A., Olivieri A.W., Crook J., Parkin R., Tchobanoglous G., Spear R.C., Eisenberg J.N.S. (2003) A risked based approach to evaluate the public health benefit of additional wastewater treatment. Environmental Science and Technology, 37(9), 1882-1891.
13. Eisenberg J.N.S., Soller J.A., Scott J., Eisenberg D.M., Colford J.M. (2004) A Dynamic Model to Assess Microbial Health Risks Associated with Beneficial Uses of Biosolids. Risk Analysis, 24(1).
14. Colford J.M.Jr., Saha S.R., Wade T.J., Wright C.C., Vu M., Charles S, Jensen P, Hubbard A, Levy D.A., Eisenberg J.N.S. (In Press) A randomized, controlled trial of an in-home drinking water intervention among HIV+ persons. Journal of Water and Health.
15. Eisenberg J.N.S., Lei X., Hubbard A.H., Brookhart, M.A., Colford Jr. J. M. (In Press) The role of disease transmission and conferred immunity in outbreaks: Analysis of the 1993 Cryptosporidium outbreak in Milwaukee. American Journal of Epidemiology

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: DR. JOSEPH EISENBERG	Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **Randomized Trial of Tapwater Treatment in the Elderly**

Source of Support: NIH/NIA
Total Award Amount: $ $2,834,113 Total Award Period Covered: 07/01/00 – 06/30/05
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **Development and application of an enteric pathogens microarray for the**

Source of Support: University Wide Aids Research Program
Total Award Amount: $ 99,600 Total Award Period Covered: 12/01/02 – 11/30/04
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **Environmental Change and Diarrheal Disease: A Natural Experiment**

Source of Support: National Institutes of Health
Total Award Amount: $ 3,089,330 Total Award Period Covered: 01/15/03 – 12/31/07
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **Determination of Health Risks Associated with the Beneficial Use of Biosolids**

Source of Support: Water Environment and Research Foundation
Total Award Amount: $ 259,988 Total Award Period Covered: 10/01/02 – 12/31/05

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **Examining epidemiologic and environmental factors associated with microbial risks**

Source of Support: Environmental Protection Agency

Total Award Amount: $ 599,757 Total Award Period Covered: 12/1/04 – 11/30/08

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: DR. JOSEPH EISENBERG

Other agencies (including NSF) to which this proposal has

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **A Randomized Control Trial of Exposure to Recreational Fresh Water**

Source of Support: National Institutes of Health

Total Award Amount: $ 3,779,151 Total Award Period Covered: 5/01/05 – 04/30/010

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer

of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

CURRICULUM VITAE of **CHARLES PETER GERBA**

EDUCATION AND DEGREES

Arizona State University, Tempe, Arizona, B. S., Microbiology, June 1969
University of Miami, Coral Gables, Florida, Ph.D., Microbiology, January 1973

POSITIONS

Postdoctoral Fellow, Department of Virology and Epidemiology, Baylor College of Medicine, Houston, Texas,1973
Assistant Professor of Environmental Virology, Department of Virology and Epidemiology, Baylor College of Medicine, Houston, Texas, 1974-1981
Associate Professor and Professor, Department of Nutrition and Food Science and University Department of Microbiology and Immunology, University of Arizona, Tucson, Arizona 1981-1990
Professor, Department of Soil, Water and Environmental Science, The University of Arizona, Tucson, Arizona 1990-
Adjunct Professor, Department of Epidemiology and Biostatistics, The University of Arizona, Tucson, Arizona, 2000-

HONORS AND AWARDS

Member, American Academy of Microbiology
Co-Recipient of Mckee Award (for outstanding contribution to groundwater protection), Water Environmental Federation 1995
Recipient of the A.P. Black Research Award for outstanding contributions to Water Science, American Water Works Association 1996
Award of Excellence in Environmental Health for outstanding and innovative research program, The National Association of Country and City Health Officials1998

PROFESSIONALLY RELATED PUBLIC SERVICE

Member - U.S. Environmental Protection Agency, Office of Drinking Water, Workshop on Revised, Drinking Water Regulations 1985
Member - Task Force for Microbiological Water, Purifier Guide Standards and Testing, Office of, Drinking Water, U.S. Environmental Protection Agency,1984-1989
Member - Drinking Water Committee, Science Advisory. Board, U.S. Environmental Protection Agency, 1987-989
Member - Working Group on Microbial Risk, Assessment. International Life Science Institute, and the United States Environmental Protection Agency 1996-2000
Member - Workshop on Water and Food Pathogen Risk Assessment, U.S. Environmental Protection Agency, and the International Life Science Institute 1999

PUBLICATIONS (more than 500 – selected publications related to proposed project)

Rose, J.B., and C.P. Gerba. 1991. Use of risk assessment for development of microbial standards. Water Sci. Technol. 24:29-34.
Rose, J.B., and C.P. Gerba. 1991. Assessing potential health risks from viruses and parasites in reclaimed water in Arizona and Florida. Water Sci. Technol. 23:2091-2098.
Regli, S., J. B. Rose, C. H. Haas, and C. P. Gerba. 1991. Modeling the risk from *Giardia* and viruses in drinking water. J. Am. Water Works Assoc. 84:76-84.

Haas, C.N., J.B. Rose, C.P. Gerba, and S. Regli. 1993. Risk assessment of virus in drinking water. *Risk Analysis*, *13*:545-552.
Rose, J.B., C.N. Haas, and C.P. Gerba. 1995. Linking microbiological criteria for foods with quantitative risk assessment. J. Food Safety. 15:121-132.
Haas, C.N., C.S. Crockett, J.B. Rose, C.P. Gerba, and A.M. Fazil. 1996. Assessing the risk posed by oocysts in drinking water. J. Am. Water Works Assoc., 88:131-136.
Gerba, C.P., J.B. Rose, and C.N. Haas. 1996. Sensitive populations: who is at the greatest risk? Int. J. Food Microbiol., 30:113-123.
Gerba, C.P., J.B. Rose, C.N. Haas, and K.D. Crabtree. 1996. Waterborne rotavirus: a risk assessment. Water Res., 30:2929-2940.
Brown, K., G. Craun, A. Dunfour, J. Eisenberg, J. Foran, C. Gauntt, C. Gerba, et al. 1996. A conceptual framework to assess the risks of human disease following exposure to pathogens. Risk Analysis 16:841-848.
Bales, R.C., L. Shimin, T.C. Jim Yeh, M.E. Lenczewski, and C.P. Gerba. 1997. Bacteriophage and microsphere transport in saturated porous media: Forced-gradient experiment at Borden, Ontario. Water Resource Research, 33:639-648.
Haas, C.H., J.B. Rose, C.P. Gerba, and C.S. Crockett. 1997. What predictive food microbiology can learn from water microbiology. Food Technology, 51:91-94.
Crabtree, K.D., C.P. Gerba, J.B. Rose, and C.N. Haas. 1997. Waterborne adenovirus: A risk assessment. Wat. Sci. Tech. 35:1-6.
Rusin, P., P. Orosz-Coughlin, and C.P. Gerba. 1998. Reduction of faecal coliform, coliform and hetrotrophic plate count bacteria in the household kitchen and bathroom by disinfection with hypochlorite cleaners. J. Appl. Microbiol. 85:819-828.
Anderson, M.A., M.H. Stewart, M.V. Yates, and C.P. Gerba. 1998. Modeling the impact of body-contact recreation on pathogen concentrations in a source drinking water reservoir. Water Res. 32:3293-3306.
Haas, C.N., J.B. Rose, and C.P. Gerba. 1999. *Quantitative Microbial Risk Assessment*. John Wiley, NY.
Dowd ,S.E., C.P. Gerba, I.L. Pepper, and S.D. Pillai. 2000. Bioaerosol transport and risk assessment in relation to the land placement of biosolids. J. Environ. Quality. 29:343-348.
Haas, C.N., A. Thayyar-Madabusi, J.B. Rose, and C.P. Gerba. 2000. Development of a dose-response relationship for *Escherichia coli* 0157:H7. Int'l J. Food Microbiology 56:153-159.
Gerba, C. P., I. L. Pepper and L. F. Whitehead. 2002. A risk assessment of emerging pathogens of concern in the land application of biosolids. Water Sci. Technol. 46:225-230.
Rusin, P., S. Maxwell and C. P. Gerba. 2002. Comparative surface-to-hand and finger-to-mounth transfer efficiency of gram positive, gram negative bacteria, and phage. J. Appl. Micobiol. 93:585-592.
Stewart, M. H., M. V. Yates, M A. Anderson, C. P. Gerba, J. B. Rose, R. De Leon and R. L, Wolfe. 2002. Predicted public health consequences of body-contact recreation on a potable water reservoir. J Amer. Water Works Assoc. 94(5): 84-97.
Chaidez, C. and C. P. Gerba. 2002. *Aeromonas hydrophila* and *Pseudomonas aeroginosa* in drinking water from various sources: a risk assessment. Res. Adv. in Water Res. 3:111-124.
Mena, K. D., C. P. Gerba, C. N. Haas, and J. B. Rose. 2003. Risk assessment of waterborne coxsackievirus. J. Amer. Water Works Assoc. 95:(7)122-132.
Brooks, J. P., C. P. Gerba and I. L. Pepper. 2004. Biological aerosol emission fate, and transport from muncipal and animal wastes. J. Residuals Sci. Technol.1:16-28.

Current and Pending Support

(See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Charles P. Gerba	Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Municipal Water Purification

Source of Support: Dept. of Homeland Security SARPA subcontract from Triton Systems, Inc.

Total Award Amount: $29,000 Total Award Period Covered: 1/1/05-6/30/05

Location of Project: Tucson, AZ

Person-Months Per Year Committed to the Project. Cal: Acad: 0.1 mm//yr

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Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Interactive UV/Ozone System as a chlorine alternative

Source of Support: Dept. of Homeland Security SARPA subcontract from Vortex Corporation

Total Award Amount: $30,000 Total Award Period Covered: 1/1/05-6/30/05

Location of Project: Tucson, AZ

Person-Months Per Year Committed to the Project. Cal: Acad: 0.1 mm/yr

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Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Development of an infectivity assay for Noroviruses in cells:

Source of Support: American Water Works Research Foundation

Total Award Amount: $400,000 Total Award Period Covered: 1/1/05-9/30/06

Location of Project: Tucson, AZ

Person-Months Per Year Committed to the Project. Cal: Acad: 0.1 mm/yr

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Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Occurrence and control of waterborne agents in the state of Arizona

Source of Support: National Science Foundation Water Quality Center/TRIF

Location of Project: Tucson, AZ

Total Award Amount: $200,000 Total Award Period Covered: 6/1/04-5/30/05

Person-Months Per Year Committed to the Project. Cal: Acad: 0.1 mm/yr

Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Assessment of the microbial water quality of individual and small systems groundwater supplies in Arizona

Source of Support: National Science Foundation Water Quality Center/TRIF

Total Award Amount: $200,000 Total Award Period Covered: 6/1/04-5/30/06

Location of Project: Pittsburgh, PA

Person-Months Per Year Committed to the Project. Cal: Acad: 0.1 mm/yr

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

USE ADDITIONAL SHEETS AS NECESSARY

Patrick L. Gurian, Ph.D.

Assistant Professor

Department of Civil, Architectural, and Environmental Engineering
Drexel University, Philadelphia, PA 19104
Phone: (215) 895-2889; Email: pgurian@drexel.edu

Experience

2004-present **Assistant Professor, Civil, Architectural, and Environmental Engineering, Drexel University.** Adjunct faculty, University of Texas School of Public Health. Current research interests include statistical modeling of human exposure to environmental contaminants and benefit-cost analysis of environmental health regulatory policies and interventional programs. Teaching interests include statistics, decision analysis, environmental chemistry, and policy analysis

2001-2004 **Assistant Professor, Civil Engineering Department, University of Texas at El Paso**, **El Paso, Texas.**

1993-1997 **Staff Engineer, McNamee, Porter, Seeley, Inc., Ann Arbor, MI.**

1990-1993 **United States Peace Corps, Community Development Engineer, Cameroon.**

Education

2001 **Carnegie Mellon University,** Ph.D. in Engineering & Public Policy, and Civil & Environmental Engineering

1990 **Stanford University,** M.S. in Environmental Engineering

1989 **Harvard University,** A.B. in Chemistry

Awards

2003 American Water Works Association Publications Award and Small Systems Division Best Paper Award (Publications Award is selected from among the divisional award winners)

1999 Herbert L. Toor Award for Outstanding Engineering and Public Policy Ph.D. Qualifying Exam Paper, "Estimating the Cost of a Revised Arsenic Drinking Water Standard."

1999 Teresa Heinz Scholarship for Environmental Research

Research Grants

"Integrated Physical-Social-Economic System Dynamics Modeling for Managing Extreme Events Induced Risk on the U.S.-Mexico Border Crossing Infrastructure," Co-PI., with Soheil Nazarian, P.I., Cesar Carrasco, Yi-Chang Chiu, and Josiah Heyman, Co-PIs., National Science Foundation, 10/2003 to 9/2006, $439,898.

"Drinking Water Consumption on the Border: A Survey of Exposure and Source Types," Center for Border Health Research, Co-P.I., with Kristina Mena (P.I.), 1/2004 to 6/2005, $73,000.

"Carbon Monoxide Exposure in Indoor Air," P.I. with Veronica Corella-Barud, Co-P.I., Southwest Center for Environmental Research and Policy, 6/2003 to 9/2004, $84,148.

"Healthy Homes for Sustainable Colonias," Co-P.I. with Steve Cook (P.I.) and Veronica Corella-Barud (Co-P.I.), State Energy Conservation Office, State of Texas, 6/2003 to 6/2004, $250,806.

"Project SPLASH in Peri-urban Communities of Ciudad Juárez," Co-P.I. with Jay Graham (P.I.) and Kristina Mena (Co-P.I.), Johnson & Johnson, 8/2002 to 8/2003, $39,997.

Peer-Reviewed Publications

Benitez-Marquez, E., B.R. Diaz, and P.L. Gurian; "Understanding the Associations Between Statewide Diabetes Prevalence and Air Pollution Emissions," *Diabetes Care, 27*(6):1515-7 (2004).

Graham, J. P., P. L. Gurian, V. Corella-Barud, R. Avilla; "Peri-urbanization and In-home Environmental Health Risks: the Side Effects of Planned and Unplanned Growth," *International Journal of Hygiene and Environmental Health* (in press).

Gurian, P.L. and J.J. Corbett; "Inland Sulfate Deposition in North America from Marine Emissions," *Transportation Research Record* (in press).

Gurian, P. L., M. J. Small, J. R. Lockwood, and M. J. Schervish. "Assessing Nationwide Cost-Benefit Implications of Multi-Contaminant Drinking Water Standards," *Journal of the American Water Works Association, 96*(3):70-83 (2004).

Lockwood J. R., M. J. Schervish, P.L. Gurian, and M. J. Small; "Analysis of Contaminant Co-occurrence in Community Water Systems," *Journal of the American Statistical Association, 99*(465):45-56 (2004).

Gurian, P. L., and M. J. Small; "Point-of-use Treatment and the Revised Arsenic MCL," *Journal of the American Water Works Association, 94*(3):101-108 (2002).

Gurian, P. L., M. J. Small, J. R. Lockwood, and M. J. Schervish; "Addressing Uncertainty and Conflicting Cost Estimates in Revising the Arsenic MCL," *Environmental Science and Technology, 35*(22):4414-4420 (2001).

Gurian, P. L., M. J. Small, J. R. Lockwood, and M. J. Schervish; "Benefit-Cost Estimation for Alternative Drinking Water MCLs," *Water Resources Research, 37*(8):2213-2226 (2001).

Lockwood, J. R., M. J. Schervish, P. L. Gurian, and M. J. Small; "Characterization of Arsenic Occurrence in U.S. Drinking Water Treatment Facility Source Waters," *Journal of the American Statistical Association, 96*(456):1184-1193 (2001).

Additional Papers

Armstrong, J., P. L. Gurian, P.L., and A. Tarquin; "Applying the Psychometric Paradigm to Understanding Public Attitudes Towards Wastewater Reuse," *Proceedings of the 19th Annual Water Reuse Symposium*, Phoenix, AZ, 2004.

Gharaibeh, N., Chiu, Y.C., and P.L. Gurian, "Fund Allocation in Transportation Infrastructure Asset Management Using Utility Analysis," submitted to *ASCE Journal of Infrastructure Systems*.

Gurian, P.L., F. Castro, Y.C. Chiu. "A Bayesian Monte Carlo Approach to Model Calibration for Queuing Systems", submitted to the 84th Annual Meeting of Transportation Research Board.

Memberships Society for Risk Analysis

Association of Environmental Engineering and Science Professors

American Water Works Association

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Patrick L. Gurian	Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Integrated Physical-Social-Economic System Dynamics Modeling for Managing Extreme Events Induced Risk on the U.S.-Mexico Border Crossing Infrastructure

Source of Support: National Science Foundation

Total Award Amount: $439,898 Total Award Period Covered: 10/1/03-9/30/06

Location of Project: University of Texas at El Paso

Person-Months Per Year Committed to the Project. 0.5 Cal: Acad: Sumr: 0.5

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Water Consumption Along the Border: Determining Intake and Source

Source of Support: Paso del Norte Health Foundation

Total Award Amount: $18,287 Total Award Period Covered: 1/04-6/05

Location of Project: University of Texas at El Paso

Person-Months Per Year Committed to the Project. 0 Cal: 0 Acad: Sumr:

Support: ☐ Current ☐ Pending ☒ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Center for Advancing Microbial Risk Assessment (CAMRA)

Source of Support: EPA-DHS via Michigan State

Total Award Amount: $2,200,000 Total Award Period Covered: 5/15/05-5/14/10

Location of Project: Drexel University

Person-Months Per Year Committed to the Project. variable Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

Curriculum Vitae of **SYED A. HASHSHAM**

ADDRESS: Department of Civil and Environmental Engineering (517) 355-8241 Phone
A-126, Research Complex-Engineering (517) 355-0250 Fax

MICHIGAN STATE UNIVERSITY HASHSHAM@EGR.MSU.EDU

East Lansing, Michigan 48824

PROFESSIONAL PREPARATION:

Ph.D. University of Illinois at Urbana-Champaign 1991-96 (Environmental Engineering and Science)
M.Tech. Indian Institute of Technology, Bombay, India 1985-86 (Environmental Science and Engineering)
B.S. Aligarh Muslim University, India 1981-84 (Civil Engineering)

RESEARCH AND PROFESSIONAL EXPERIENCE:

1999- Present: Assistant Professor, Department of Civil and Environmental Engineering Michigan State University
1999- Present: Adjunct Assistant Professor, Center for Microbial Ecology
1998-99: Stanford University, Stanford, CA, Post-doctoral Research Associate
1996-98: Michigan State University, E. Lansing, MI, Post-doctoral Research Associate and Lecturer
1991-96: University of Illinois at Urbana-Champaign, IL, Graduate Research/ Teaching Assistant
1990-91: University of Texas at Arlington, TX, Graduate Teaching Assistant
1986-90: Aligarh Muslim University, Aligarh, India, Lecturer
1985-86: Indian Institute of Technology, Bombay, India, Project Assistant

RESEARCH INTERESTS:

Development of microarrays for water safety, human health, and quantitative environmental genomics; Mathematical modeling of molecular data related to microbial communities.

PUBLICATIONS:

1. Hashsham, S.A., Wick, L.M., Rouillard, J-M., Gulari, E., and J.M. Tiedje, 2004. Potential of DNA microarrays for developing parallel detection tools (PDTs) for microorganisms relevant to biodefense and related research needs. *Biosensors and Bioelectronics*. In Press; Available online September 2; 2004.

2. Hashsham, S.A. S. Callister, and M. Tijdens. Oligonucleotide probe design for mixed microbial community microarrays and other applications and important considerations for data analysis. *Molecular Microbial Ecology Manual*. 2nd Edition, Kluwer Academic Publishers, The Netherlands. 1.7.8:1-26, 2004.

3. Hashsham, S.A., Alm, E.W., Stedtfeld, R.D., Traver, R.G., and M. Duran. Detection and occurrence of indicator organisms and pathogens. *Water Environment Research*. Vol. 75, No. 6. 2004.

4. Jenkins, T.M., T.M. Scott, J.R. Cole, S.A. Hashsham, and J.B. Rose, Assessment of virulence-factor activity relationships (VFARs) for waterborne diseases. *Water Science and Technology*. 50(1):309-314. 2004.

5. Denef VJ, Park J, Tsoi TV, Rouillard JM, Zhang H, Wibbenmeyer JA, Verstraete W, Gulari E, Hashsham SA, Tiedje JM., Biphenyl and benzoate metabolism in a genomic context: outlining genome-wide metabolic networks in *Burkholderia xenovorans* LB400., *Applied and Environmental Microbiology.* 70 (8):4961-70. 2004.

6. Dollhopf SL, Pariseau ML, Hashsham SA, Tiedje J.M., Competitive and cooperative interactions affecting a fermentative spirochete in anaerobic chemostats. *Microbial Ecology.* 46 (1): 1-11. 2003.

7. Callister, SJ., Ayala-del-Rio H.L., and S.A. Hashsham. Quantification of a single population in a mixed community using a laser integrated microarray scanner. *Environmental Engineering and Science.* 2(4):247-253. 2003.

8. Hashsham, S.A. and D.L. Freedman, Adsorption of vitamin B_{12} to alumina, kaolinite, sand and sandy soil. *Water Research.* 37: 3189-3193. 2003.

9. Musarrat J., and S.A. Hashsham. Customized cDNA microarray for expression profiling of environmentally important genes of *Pseudomonas stutzeri* strain KC. *Teratogenesis Carcinogenesis and Mutagenesis.* 283-294. Suppl. 2003.

10. Denef, V.J., J. Park, J.L.M. Rodrigues, T.V. Tsoi, S.A. Hashsham and J.M. Tiedje. Validation of a more sensitive method for using spotted oligonucleotide DNA microarrays for functional genomics studies on bacterial communities. *Environmental Microbiology.* 5 (10), 933-943. 2003.

11. Sun, B., B.M. Griffin, R.K. Kehrer, S.A. Hashsham, and J.M. Tiedje. Microbial reductive dechlorination of 1,1,1-trichloroethane to chloroethane, *Science.* 298: 1023. 2002.

12. Dollhopf, S.L., S.A. Hashsham S. A., F.B. Dazzo, R.F. Hickey, C.S. Criddle, and J.M. Tiedje. The impact of fermentative organisms on carbon flow in methanogenic systems under constant low-substrate conditions. *Applied Microbiology and Biotechnology.* 56: 531-538. 2001.

13. Dollhopf, S.L., S.A. Hashsham, and J.M. Tiedje. Interpreting 16S rDNA T-RFLP Data: Application of self-organizing maps and principal component analysis to describe community dynamics and convergence. *Microbial Ecology***.** 42 (4): 495-505. 2001.

14. Fernandez, A., S. Hashsham, S. Dollhopf, L. Raskin, O. Glagoleva, F. Dazzo, R. Hickey, C. Criddle, and J. Tiedje. Flexible community structure correlates with stable community function in methanogenic bioreactor communities perturbed by glucose. *Applied and Environmental Microbiology*. 66 (9):4058-4067. 2000.

15. Hashsham S., A. Fernandez, S. Dollhopf, F. Dazzo, R. Hickey, J. Tiedje, and C. Criddle. Parallel processing of substrate correlates with greater functional stability in methanogenic bioreactor communities perturbed by glucose. *Applied and Environmental Microbiology*. 66 (9):4050-4057. 2000.

16. Hashsham, S.A. and D.L. Freedman. Enhanced biotransformation of carbon tetrachloride by *Acetobacterium woodii* upon addition of hydroxocobalamin and fructose. *Applied and Environmental Microbiology*. 65(10): 4537-4542. 1999.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Syed Hashsham
Michigan State University

Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Real time Scanning and Hybridization Capabilities at MSU for Quantitative and Parallel Microorganisms on DNA

Source of Support: Department of Defense
Total Award Amount: $150,495 Total Award Period Covered: 2004-2005
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. .09 Cal: Acad: .09 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Health Hazards from Groundwater Contamination

Source of Support: NIH
Total Award Amount: $1,244,577 Total Award Period Covered: 4/1/00-3/31/05
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. 0.9 Cal: Acad: .9 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Evaluation of Remediation at Schoolcraft Plume G and F Contaminated with Chlorinated Solents and Metals

Source of Support: Michigan Department of Environmental Quality
Total Award Amount: $250,410 Total Award Period Covered: 1/1/00-12/31/05
Location of Project: Schoolcraft, MI
Person-Months Per Year Committed to the Project. Cal: Acad: .27 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Bioreactor Landfill Field Evaluation in Harrison, MI

Source of Support: Department of Energy and Environmental Research and Education

Total Award Amount: $207,000 Total Award Period Covered: 6/18/04-5/30/04

Location of Project: Harrison, MI

Person-Months Per Year Committed to the Project. Cal: Acad: .36 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Characterization and Application of Reductive Dehalogenase Genes in Enhancement and Monitoring of

Biodegradation of Chlorinated Pollutants

Source of Support: EPA

Total Award Amount: $469,154 Total Award Period Covered: 8/1/02-7/31/04

Location of Project: East Lansing, MI

Person-Months Per Year Committed to the Project. Cal: Acad: .45 Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Syed Hashsham
Michigan State University

Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Development of Microarrays for Evaluating Phylogenetic and Functional Diversity of he Microbial World

Source of Support: NSF

Total Award Amount: $25,000 Total Award Period Covered: 8/1/02-7/31/05

Location of Project: East Lansing, MI

Person-Months Per Year Committed to the Project. Cal: Acad: .45 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Bioinformatics Pilot Program for the Assessment of Virulence Factors and Activity Relationships (VFARs) for

Waterborne Diseases
Source of Support: EPA
Total Award Amount: $95,786 Total Award Period Covered: 9/1/02-9/30/04
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. Cal: Acad: .45 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Flexible Biochip for Highly Parallel Microbial Detection

Source of Support: NIH-NCRR
Total Award Amount: $1,370,788 Total Award Period Covered: 8/1/03-7/31/06
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. Cal: Acad: 1.8 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Emerging Microbial Indicator Technologies

Source of Support: EPA
Total Award Amount: $20,495 Total Award Period Covered: 9/15/03-8/27/04
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. Cal: Acad: .9 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Pilot Scale Evaluation of Sustainable Manure Management by Struvite Recovery

Source of Support: National Center for Manure Management
Total Award Amount: $35,000 Total Award Period Covered: 8/1/01-1/31/05
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. Cal: Acad: .45 Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Other agencies (including NSF) to which this proposal has

Investigator: Syed Hashsham
Michigan State University

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

GeneScreen: A Low Cost and High Density DNA Biochip for Detecting up to 30,000 Microorganisms

Source of Support: Michigan Economic Development Corporation
Total Award Amount: $881,561 Total Award Period Covered: 9/8/03-9/7/06
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. Cal: Acad: 1.44 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Probing Microbial Communities by Stable Isotope and RNA/DNA Analyses

Source of Support: NIEHS
Total Award Amount: $223,804 Total Award Period Covered: 9/30/03-7/31/05
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. Cal: Acad: .45 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Evaluation of Landfill Gas Emissions from an Instrumented Bioreactor Landfill Cell

Source of Support: NSF
Total Award Amount: $43,772 Total Award Period Covered: 7/1/03-6/30/05
Location of Project: Harrison, MI
Person-Months Per Year Committed to the Project. Cal: Acad: .09 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Development of a Virulence Factor biochip and its Validation for Microbial Risk Assessment in Drinking Water

Source of Support: EPA
Total Award Amount: $600,000 Total Award Period Covered: 9/1/04-8/31/07
Location of Project: East Lansing, MI
Person-Months Per Year Committed to the Project. Cal: Acad: .63 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near ☐

Future *Transfer of Support

Project/Proposal Title:

Development of Aeration Strategy for Elevating Temperature in Bioreactor Landfill

Source of Support: Waste Management, Inc.

Total Award Amount: $96,545 Total Award Period Covered: 3/1/04-2/28/05

Location of Project: East Lansing, MI

Person-Months Per Year Committed to the Project. Cal: Acad: .27 Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

BIOGRAPHICAL SKETCH

NAME Paul S. Keim POSITION TITLE

The Cowden Endowed Chair in Microbiology

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	YEAR(s)	FIELD OF STUDY
Northern Arizona University, Flagstaff AZ	B.S.	1975-77	Biology and Chemistry
University of Kansas, Lawrence KS	Ph.D.	1977-81	
University of Utah, Salt Lake City UT	Postdoctoral	1981-87	Plant Biochemist
Iowa State University, Ames IA	Postdoctoral	1987-88	

A. Positions and Honors

Research and Professional Experience

1981-4 Research Associate, Dept of Biology, University of Utah (K.G. Lark, mentor)
1984-7 Research Assistant Professor of Biology, University of Utah
1987-8 Research Associate, Iowa State University, Dept. of Genetics
1989-2 Assistant Professor of Biology, Northern Arizona University
1992-5 Associate Professor of Biology with Tenure, Northern Arizona University
1995-6 Professor of Biological Sciences, Northern Arizona University
1992- Affiliate Researcher (Q), BioSciences - Los Alamos National Laboratory
1998- Project Director - Howard Hughes Medical Institute: *Project BioConnect*
1998- Adjunct Faculty - College of Veterinary Medicine - Louisiana State University
1997- The E. Raymond and Ruth Cowden Endowed Chair in Microbiology, NAU
2002- Arizona Regents Professor, Northern Arizona University
2003- Director of Pathogen Genomics, TGen (Phoenix AZ)

Honors and Awards

Bachelor of Science, *magna cum laude* Biology & Chemistry (1977)
Phi Kappa Phi (1977)
Ph.D. Dissertation awarded Honors in Plant Biochemistry (1981)
"Hot Paper" selection by *The Scientist* (1990)
Phi Kappa Phi - NAU Faculty Scholar of the Year (1995)
The Centennial Distinguished Professor- NAU College of A&S (1998)
The Betty Klepper Honorary Scholar – Crop Science Society (2001)
Fellow, American Academy of Microbiology (2002)

B. Selected Publications from 133 Total (54 published since 2000)

Pearson, T., J. Busch, J. Ravel, T. Read, S. Rhoton, J. U'Ren, T. Simonson, S. Kachur, R. Leadem, M. Cardon, M. Van Ert, L. Huynh, C. Fraser & P. Keim. Phylogenetic discovery bias in *Bacillus anthracis* using single-nucleotide polymorphisms from whole-genome sequencing. *PNAS (USA)* **101**:13536-13541.

Johansson, A., J. Farlow, P. Larsson, M. Dukarich, E. Chambers, M. Byström, J. Fox, M. Chu, M. Forsman, A. Sjöstedt, & P. Keim. 2004. Worldwide genetic relationships among *Francisella tularensis* isolates determined by multiple-locus variable-number tandem repeat analysis. *Journal of Bacteriology* **186:**5808-5818.

Girard, J.M., D.M. Wagner, A.J. Vogler, C. Keys, C.J. Allender, L.C. Drickamer, & P. Keim. 2004. Differential plague transmission dynamics determine *Yersinia pestis* population genetic structure on local, regional, and global scales. *PNAS (USA)* **101**:8408-8413. (cover photo).

Keim, P., M. Van Ert, T. Pearson, A. Vogler, L. Huynh, & D. Wagner. 2004. Anthrax molecular epidemiology and forensics: using the appropriate marker for different evolutionary scales. Infection, Genetics and Evolution ***4****:205-213.*

Hill, K.K., L.O. Ticknor, M. Asay, H. Blair, K. Bliss, M. Laker, P.E. Pardington, A.P. Richardson, M. Tonks, J.D. Kemp, A-B. Kolstø, A.C.L. Wong, P. Keim, & P.J. Jackson. 2004. Fluorescent amplified fragment length polymorphism analysis of *Bacillus anthracis*, *Bacillus cereus*, and *Bacillus thuringiensis* isolates. *Applied Environmental Microbiology* **70**:1068-1080.

Takahashi, H., P. Keim, A.F. Kaufmann, K.L. Smith, C. Keys, K. Taniguchi, S. Inouye, & T. Kurata. 2004. *Bacillus anthracis* incident, Kameido, Tokyo, 1993. *Emerging Infectious Diseases*. **10:**117-120.

Price, L.B., A. Vogler, T. Pearson, J.D. Busch, J.M. Schupp, & P. Keim. 2003. *In vitro* selection and characterization of *Bacillus anthracis* mutants with high-level resistance to ciprofloxacin. *Antimicrobial Agents and Chemotherapy* **47**:2362-2365.

Farlow, J., D. Postic, K.L. Smith, Z. Jay, G. Baranton, & P. Keim. 2002. Strain typing of *Borrelia burgdorferi, B. afzelii,* and *B. garinii* by using multiple-locus variable-number tandem repeat analysis. *Journal of Clinical Microbiology* **40**:4612–4618.

Fouet, A., K.L. Smith, C. Keys, J. Vaissaire, C. Le Doujet, M. Lévy, M. Mock, & P. Keim. 2002. Diversity among French *Bacillus anthracis* isolates. *Journal of Clinical Microbiology* **40:** 4732–4734.

Read, T.D., S.L. Salzberg, M. Pop, M. Shumway, L. Umayam, L. Jiang, E. Holtzapple, J. Busch, K.L. Smith, J.M. Schupp, D. Solomon, P. Keim, & C.M. Fraser. 2002. Comparative genome sequencing for discovery of novel polymorphisms in *Bacillus anthracis*. *Science* **296**:2028-2033.

Keim, P, K.L. Smith, C. Keys, H. Takahashi, T. Kurata, & A. Kaufmann. 2001. Molecular investigation of the Aum Shinrikyo anthrax release in Kameido, Japan. *Journal of Clinical Microbiology* **39**:4566-4567.

Vogler, A.J., J.D. Busch, S. Percy-Fine, C.M. Tipton-Hunton, K.L. Smith, & P. Keim. 2001. Molecular analysis of rifampicin resistance in *Bacillus anthracis* and *B. cereus. Antimicrobial Agents and Chemotherapy* **46**:511-513.

Farlow, J., K.L. Smith, J. Wong, M. Abrahms, M. Lytle, & P. Keim. 2001. *Fransicella tularensis* strain typing using multiple-locus variable number tandem repeat analysis. *Journal of Clinical Microbiology* **39**:3186-3192.

Klevytska, A.M., L.B. Price, J.M. Schupp, P.L. Worsham, J. Wong, & P. Keim. 2001. Identification and characterization of variable-number tandem repeats in the *Yersinia pestis* genome. *Journal of Clinical Microbiology* **39:**3179-85.

Smith, K.L., V. DeVos, H. Bryden, L.B. Price, M.E. Hugh-Jones, & P. Keim. 2000. *Bacillus anthracis* diversity in Kruger National Park. *Journal of Clinical Microbiology* **38**:3780-3784.

Schupp, J.M., A. M. Klevytska, L.B. Price, and P. Keim. 2000. *vrrB*, A hypervariable open reading frame in *Bacillus anthracis*. *Journal of Bacteriology* **182**:3989-3997.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Paul Keim

Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Characterization of the CDC Y. pestis and F. tularensis Strain Archive

Source of Support: DHS

Total Award Amount: $194,068 Total Award Period Covered: 10/1/02-9/30/05

Location of Project: CDC-Ft. Collins and Northern Arizona University

Person-Months Per Year Committed to the Project. Cal: 0.50 Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Acquisition of a High Capacity Genotyping Facility for Diverse Biological Applications

Source of Support: NSF

Total Award Amount: $581,812 Total Award Period Covered: 07/01/03-06/30/05

Location of Project: Northern Arizona University

Person-Months Per Year Committed to the Project. 0.00 Cal: 0.00 Acad: 0.00 Sumr: 0.00

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: MLVA: A High Resolution Approach for Molecular Typing of Bacterial Pathogens

Source of Support: DHS

Total Award Amount: $1,100,000 Total Award Period Covered: 01/01/04-12/31/05

Location of Project: Northern Arizona University

Person-Months Per Year Committed to the Project. Cal: 1.0 Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Molecular Epidemiology and Evolution of Bacillus anthracis

Source of Support: NIH-NIAID
Total Award Amount: $1,150,000 Total Award Period Covered: 05/01/00-04/30/05
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. Cal: Acad: 1.0 Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Comparison of B. anthracis Genomes from Diverse Strains

Source of Support: NIH-NIAID from TIGR subcontract
Total Award Amount: $530,000 Total Award Period Covered: 08/01/02-07/30/05
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. Cal: 0.25 Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Paul Keim

Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: BDAP: Biological Demonstration Project

Source of Support: DOE: NNSA-CBNP
Total Award Amount: $300,000 Total Award Period Covered: 04/01/03-03/31/05
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. Cal: 1.0 Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:
Centers for Public Health Preparedness

Source of Support: CDC-HHS
Total Award Amount: $421,589 Total Award Period Covered: 08/31/03-08/30/05
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. Cal: 1.00 Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Plant Genetic Structure as a Controlling Factor in Community and Ecosystem Functioning: Natural and Synthetic Hybrids of a Dominant Tree

Source of Support: NSF
Total Award Amount: $3,000,000 Total Award Period Covered: 10/01/00-09/30/05
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. Cal: 1.0 Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: FIBR Community Genetics, Heritability & Evolution: Consequences of Extended Phenotypes

Source of Support: NSF
Total Award Amount: $4,981,000 Total Award Period Covered: 09/01/04-08/31/09
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. Cal: Acad: 0.5 Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: High-Resolution and Highly Sensitive Assays for Bacterial Threat Agents

Source of Support: DHS-HSARPA
Total Award Amount: $888,188 Total Award Period Covered:
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. 3.0 Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Paul Keim

Other agencies (including NSF) to which this proposal has

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Regional Center of Excellence - Region IX

Source of Support: NIH - NIAID
Total Award Amount: $1,499,490 Total Award Period Covered:
Location of Project: Northern Arizona University
Person-Months Per Year Committed to the Project. 1.0 Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME **James S. Koopman**	POSITION TITLE Full Professor with tenure

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Michigan, Ann Arbor, MI	B.S.	1969	Biology
University of Michigan, Ann Arbor, MI	M.D.	1969	Medicine
University of California, Los Angeles, CA	DIPLOMA	1972	Pediatrics
University of Washington, Seattle, WA	M.P.H.	1976	Epidemiology

Positions and Honors.

1970-1972 Pediatrics residence at Harbor General Hospital, Los Angeles, CA.
1972-1974 Epidemic Intelligence Service Officer in the State of Washington. Established an immunization program, computerized surveillance data, and acted as state epidemiologist.
1974 WHO consultant with the smallpox eradication program in India.
1974-1976 Studies at the University of Washington leading to an MPH including Biostatistics, modeling and demography.
1975-1978 Diarrheal disease and nutrition investigations in Cali, Columbia as visiting scientist with CIDEIM
1978-1983 Assistant Professor of Epidemiology, University of Michigan.
1983-1991 Associate Professor at the University of Michigan.
1984-1986 On leave from the University. CDC consultant in Mexico establishing an Epidemiologic Investigations Service and Epidemiology Residency at the national level in the Mexican Secretariate of Health.
1991- Full Professor, Department of Epidemiology, University of Michigan. Dedicated to developing a systems science of infection transmission
1995- Founding member and leader of activities related to infection transmission modeling, University of Michigan, Center for the Study of Complex Systems

C. Selected peer-reviewed publications (in chronological order).

1. **Koopman JS**, Prevots DR, Vaca-Marin MA, Gomez-Dantes H, Zarate ML, Longini IM, Sepulveda J. Determinants and predictors of dengue infection in Mexico. Am J Epidemiol. 1991; 133(1): 1168-78.
2. **Koopman JS**, Simon CP, and Jacquez JA. Assessing contagiousness effects of vaccines and risk factors for transmission. In Modeling the AIDS Epidemic: Planning, Policy, and Prediction, Kaplan EH and Brandeau ML (Eds.) 1994; p. 439-460.
3. **Koopman JS** and Longini IM. Ecological effects of individual exposures and non-linear disease dynamics in populations. Amer J Pub Hlth. 1994; 84(5):836-842.
4. Jacquez JA, Simon CP, and **Koopman JS**. Core groups and the R_O's for subgroups in SIS and SI models. In Epidemic Models: Their Structure and Relationship to Data. Mollison D.(ed.) Camb. Univ. Press. 1995; p. 279-301.
5. Jacquez JA, **Koopman JS**, Simon CP, and Longini IM. Role of the primary infection in epidemics of HIV infection in gay cohorts. JAIDS. 1994; 7:1169-1184.
6. **Koopman JS** and Little RJ. Assessing HIV vaccine effects. Amer J Epidemiol. 1995; 142(10):1113-1120.
7. **Koopman JS**. Emerging objectives and methods in epidemiology. Amer J Pub Health. 1996; 86(5):630-632.
8. **Koopman JS**, Simon CP, and Jacquez JA. Data analysis for estimating risk factor effects using transmission models. In Models for Infectious Human Disease, Isham and Medley (Eds.) 1996; pg. 290-291.

9. Simon CP, Jacquez JA, and **Koopman JS**. A Liapunov function approach to computing R_o. In Models for Infectious Human Disease, Isham and Medley (Eds.) 1996; pg. 311-314.
10. **Koopman JS**, Jacquez JA, Simon CP, Foxman B, Pollock S, Barth-Jones D, Adams A, Welch G, Lange K. The role of primary HIV infection in the spread of HIV through populations. JAIDS and HR. 1997; 14:249-258.
11. Adams A., Barth-Jones DC, Chick SE, **Koopman JS**. Simulations to Evaluate HIV Vaccine Trial Methods. Simulation. 1998; 71(4):228-241.
12. **Koopman JS**, Lynch JW. Individual Causal Models and Population System Models in Epidemiology. J Amer Public Health Assoc. 1999; 89:1170-4.
13. **Koopman JS**, Chick SE, Riolo CS, Adams AL, Wilson ML, Becker MP. Modeling Contact Networks and Infection Transmission in Geographic and Social Space Using GERMS. Sex. Transm. Dis. 27. 2000; 617-626.
14. Chick SE, Adams AL, **Koopman JS**. Analysis and simulation of a stochastic, discrete-individual model of STD transmission with partnership concurrency. Mathematical Biosciences. 2000; 166(1):45-68.
15. Chick, S.E., **Koopman, JS**. Soorapanth, S., Brown, M.E. Infection Transmission System Models for Microbial Risk Assessment, The Science of the Total Environment. 2001; 274(1-3, June): 197-207.
16. Riolo, C.S., **Koopman, JS**. Chick, S.E., Methods and measures for the description of epidemiologic contact networks. J Urban Health: Bulletin of the New York Academy of Sciences. 2001; 78: 446-457.
17. Chick SE, Barth-Jones DC, **Koopman JS**. Bias reduction for risk ratio and vaccine effect estimators. Statistics in Medince. 2001; 20: 1609-1624.
18. Simon CP, **Koopman JS**. Infection Transmission Dynamics and Vaccination Program Effectiveness as a Function of Vaccine Effects in Individuals. Mathematical Approaches for Emerging and Reemerging Infectious Diseases: Models, Methods and Theory Ed. S Blower,C Castillo-Chavez,P van den Driessche, AA Yakubu. Springer,New York,2002,143-157.
19. **Koopman JS**, Chick SE, Riolo CP, Simon CP, Jacquez G. Stochastic effects on endemic infection levels of disseminating versus local contacts. Mathematical Biosciences. 2002; 180:49-71.
20. **Koopman JS**, Jacquez G, Chick SE. New Data and Tools for Integrating Discrete and Continuous Modeling Strategies. In Population Health and Aging: Strengthening the Dialogue between Epidemiology and Demography. M Weinstein, AI Hermalin, MA Stoto eds. Annals of the New York Academy of Sciences. 2001; 954:268-294.
21. Soorapanth S, Chick SE, **Koopman JS**. Simulation of Stochastic Infection Transmission Models Designed to Inform Water Treatment Decisions, In N. Giambiasi, C. Frydman, eds., Proc. European Simulation Symposium. Society for Computer Simulation. 2001; p. 517-521.
22. **Koopman JS**. Modeling Infection Transmission -The Pursuit of Complexities That Matter. Epidemiology. 2002; 13(6):622-624.
23. **Koopman JS,** Chick SE, Simon CP, Riolo CS, Jacquez G. Stochastic effects on endemic infection levels of disseminating versus local contacts. Mathematical Biosciences. 2002; 180: 49-71.
24. **Koopman JS**. Controlling Smallpox. Science. 2002; 298: 1342-1344.
25. **Koopman JS**, Lin X, Chick SE, Gilsdorf J. Transmission Model Analysis of Nontypeable *Haemophilus influenzae* Immunity Effects on Transmission and Pathogenicity. in Handbook of Operations Research / Management Science Applications in Health Care Ed. F Sainfort, M Brandeau, W Pierskalla. Kluwer. March 2004.
26. Chick SE, Soorapanth S**, Koopman JS**. Microbial Risk Assessment for Drinking Water. In Handbook of Operations Research / Management Science Applications in Health Care Ed. F Sainfort, M Brandeau, W Pierskalla. Kluwer. March 2004.
27. Chick, SE, **Koopman, JS,** Soorapanth, S, 2003, Inferring Infection Transmission Parameters That Influence Water Treatment Decisions. Management Science. 2003; 49(7): 920-935.
28. **Koopman, JS**. Modeling Infection Transmission. Annu. Rev. Public Health. 2004; 25: 303-326..
29. Riggs TW, **Koopman JS.** A Stochastic Model of vaccine trials for endemic infections using group randomization. Epidemiol. Infect 2004, 132 (4), currently available on-line while in print.
30. Jacobsen KH, **Koopman JS**. Declining hepatitis A seroprevalence: a global randomization. Epidemiol. Infect 2005; 133, currently available on-line while in print.
31. **Koopman JS**, Simon CP, Riolo CP. When to Control Endemic Infections by Focusing on High-Risk Groups. Epidemiology 2004. pending publication.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this

Investigator: James Koopman	Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Integrating Phylogeny, Physics, and Epidemiology Models for Infection Control

Source of Support: Rackham Interdisciplinary Collaboration Research Grant

Total Award Amount: $250,000 Total Award Period Covered: 09/01/02-08/31/05

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Emerging Infection Control Lessons from Beijing SARS

Source of Support: NIH

Total Award Amount: $3,332,739 Total Award Period Covered: 07/01/05-06/30/10

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.

NAME	POSITION TITLE
Nicas, Mark	Adjunct Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
City College of New York	B.S.	1968	Biology/Chemistry
University of Wisconsin	M.S.	1974	Genetics
University of California, Berkeley	M.P.H.	1984	Env. Health Sciences
University of California, Berkeley	Ph.D.	1991	Env. Health Sciences

A. Positions and Honors

Positions and Employment

1977-1981 Industrial Hygienist, OSHA, U.S. Department of Labor, Cincinnati, OH, and Milwaukee, WI
1982 Industrial Hygienist, International Union of Electrical Workers, AFL-CIO, Washington, D.C.
1983 Industrial Hygienist, Wisconsin Department of Health and Social Services, Madison,WI
1985-1987 Industrial Hygienist, California Department of Industrial Relations, San Francisco, CA
1988-1993 Industrial Hygienist, California Department of Health Services, Berkeley, CA
1993-1995 Lecturer, School of Public Health (SPH), University of California, Berkeley
1996-1997 Adjunct Assistant Professor, SPH, University of California, Berkeley
1998-present Adjunct Associate Professor, SPH, University of California, Berkeley
2002-present Industrial Hygiene Program Director, SPH, University of California, Berkeley

Professional Memberships

1977-present American Industrial Hygiene Association (AIHA)
1997-present Society for Risk Analysis
2004-American Biological Safety Association
1991-present Exposure Assessment Strategies Committee, AIHA
1986-present Diplomate #3462, American Board of Industrial Hygiene, Comprehensive Practice

Honors

1967 Phi Beta Kappa
1968 Magna Cum Laude
1991 Michigan Industrial Hygiene Society Award, Best Paper in the AIHA Journal
1992 John M. White Award, AIHA Respiratory Protection Committee
2001 Edward J. Baier Technical Achievement Award, AIHA
2003 Fellow, AIHA

B. Selected peer-reviewed publications related to microbial risk assessment

1. **Nicas M**, A Hubbard, R Jones and A Reingold (2004): The Infectious Dose of Variola (Smallpox) Virus, *J. Appl. Biosafety 9*:118-127
2. **Nicas M**, W Charney, R Harrison and B Borwegen (2004): Respiratory Protection and Severe Acute Respiratory Syndrome, *J. Occup. Environ. Med. 46*:195-197
3. **Nicas M** and A Hubbard (2003): A Risk Analysis Approach to Selecting Respiratory Protection against Airborne Pathogens Used for Bioterrorism, *Am. Ind. Hyg. Assoc. J. 64*:95-101
4. **Nicas M** and A Hubbard (2002): A Risk Analysis for Airborne Pathogens with Low Infectious Doses: Application to Respirator Selection against Coccidioides immitis Spores, *Risk Analysis 22*:1153-1163
5. **Nicas M**, J. Neuhaus and R.C. Spear (2000): Risk-Based Selection of Respirators against Infectious Aerosols: Application to Anthrax Spores, *J. Occup. Environ. Med. 42*:737-748
6. **Nicas M** (2000): Regulating the Risk of Tuberculosis Transmission among Health Care Workers, *Am. Ind. Hyg. Assoc. J. 61*:334-339
7. Sutton P, **M Nicas** and RJ Harrison (2000): Tuberculosis Isolation: Comparison of Written Procedures and Actual Practices in Three California Hospitals, *Infect. Control Hosp. Epidemiol. 21*:28-32
8. **Nicas M** and S Miller (1999): A Multi-Zone Model Evaluation of the Efficacy of Upper-Room Air Ultraviolet Germicidal Irradiation, *Appl. Occup. Environ. Hyg. 14*:317-328
9. Nazaroff W, **M Nicas** and S Miller (1998): Framework for Evaluating Measures to Control Nosocomial Tuberculosis Transmission, *Indoor Air 8*:205-218
10. Sutton P, **M Nicas**, F Reinisch and RJ Harrison (1998): Evaluating the Control of Tuberculosis among Healthcare Workers: Adherence to CDC Guidelines of Three Urban Hospitals in California, *Infect. Control Hosp. Epidemiol*. *19*:487-493
11. **Nicas M** (1998): A Risk/Cost Analysis of Alternative Screening Intervals for Occupational Tuberculosis Infection, *Am. Ind. Hyg. Assoc. J. 59*:104-112
12. **Nicas M** (1998): Assessing the Relative Importance of the Components of an Occupational Tuberculosis Control Program, *J. Occup. Environ. Med*. *40*:648-654
13. **Nicas M** and E Seto (1997): A Simulation Model for Occupational Tuberculosis Transmission, *Risk Analysis 17*:606-616
14. **Nicas M** (1996): Refining A Risk Model for Occupational Tuberculosis Transmission, *Am. Ind. Hyg. Assoc. J. 57*:16-22
15. **Nicas M** (1996): An Analytical Framework for Relating Dose, Risk and Incidence: An Application to Occupational Tuberculosis Infection, *Risk Analysis 16*:527-538
16. **Nicas M** (1995): Respiratory Protection and the Risk of *Mycobacterium tuberculosis* Infection. *Am. J. Ind. Med. 27*:317-333
17. **Nicas M** (1994): Modeling Respirator Penetration Values with the Beta Distribution: An Application to Occupational Tuberculosis Transmission. *Am. Ind. Hyg. Assoc. J. 55*:515-524

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Mark Nicas University of California-Berkeley	Other agencies (including NSF) to which this proposal has

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Risk Assessment for Airborne Pathgens used for Bioterrorism

Source of Support: ASPH/NIOSH/CDC

Total Award Amount: $130,686 Total Award Period Covered: 08/01/04-7/31/05

Location of Project: Berkeley, CA

Person-Months Per Year Committed to the Project. 6 Cal: X Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Health Protective Textiles: Bridging the Disposable/Reusable Divide

Source of Support: NSF

Total Award Amount: $95,884 Total Award Period Covered: 09/15/04-09/14/09

Location of Project: Berkeley, CA

Person-Months Per Year Committed to the Project. 2.4 Cal: X Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Protecting Lithographic Printers from Chronic Health Damage

Source of Support: California Department of Health Services

Total Award Amount: $55,566 Total Award Period Covered: 08/30/04-06/30/05

Location of Project: Berkeley, CA

Person-Months Per Year Committed to the Project. 0.6 Cal: X Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Occupational Safety and Health Training Grant- Northern California Educational Resource

Source of Support: NIOSH
Total Award Amount: $939,000 Total Award Period Covered: 07/01/04-06/30/05
Location of Project: Berkeley, CA
Person-Months Per Year Committed to the Project. 3 Cal: X Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

MITCHELL J. SMALL
Departments of Civil & Environmental Engineering and Engineering & Public Policy
Carnegie Mellon University
Pittsburgh, PA 15213-3890 tel: 412-268-8782 fax: 412-268-7813
E-mail: ms35@andrew.cmu.edu
Born: June 11, 1953, Pittsburgh, Pennsylvania US Citizenship
Social Security Number: 185-40-2218

Education

1975 BS in Civil Engineering/Engineering and Public Affairs, Carnegie-Mellon University
1979 MS in Environmental and Water Resources Engineering, University of Michigan
1982 Ph.D. in Environmental and Water Resources Engineering, University of Michigan

Current and Previous Positions

H. John Heinz III Professor of Environmental Engineering, 2001 – present.
Professor, Civil & Environmental Engineering/Engineering & Public Policy, Carnegie Mellon University, 1991 - present. (Associate Professor, 1987-1991; Assistant Professor, 1982 - 1987.)
-Associate Department Head for Graduate Education, Engineering & Public Policy, 1992-present.
-Director of Environmental Engineering Minor, 1992- 1997.
-Acting Department Head, Engineering & Public Policy, January 1997 - September, 1997.
Adjunct Professor of Environmental and Occupational Health, University of Pittsburgh Graduate School of Public Health, 1995 - present.
Engineer, Hydroscience, Inc., 1975-1978

Recent Professional Activities

Member of EPA Science Advisory Board (SAB), Environmental Engineering Committee, 1985-1991; Consultant to SAB, 1991-present; Chair of SAB Environmental Models Subcommittee, 1999-present.
Member of EPA ORD Board of Scientific Counselors (BOSC), 1996 - 2002
Member of National Research Council Committees:
- Hazardous Wastes in Highway Rights-of-Way, 1990-1993
- Remediation Priorities for Hazardous Waste Sites, 1991-1994
- USGS Water Resources Research, 1993-1996.
- Risk Characterization, 1994-1996.
- Environmental Remediation at Naval Facilities, 2000 - 2002.

Associate Editor, *Environmental Science & Technology*, Policy Analysis section, 1995-present.
Elected Councilor, Society for Risk Analysis (SRA), 1999-2002.
Chair of DOE Independent Peer Review Committee for Multimedia Models for Use in Programmatic Environmental Impact Statement Risk Assessment, 1994.

Awards and Fellowships

Elected Fellow, Society for Risk Analysis (SRA), 2003
American Water Works Association (AWWA) Best Paper Award, 2002, for "Point-of-use treatment and the revised arsenic MCL."
Frank Wilcoxon Prize, 1992, American Society for Quality Control, for best practical applications paper in Technometrics, "Modeling lake-chemistry distributions: Bayesian methods for estimating a finite-mixture model."
National Science Foundation Presidential Young Investigator Award, 1986-1991.

Research Interests

Environmental Health Risk Assessment: statistical methods and uncertainty analysis; human exposure modeling; drinking water quality and regulation; human risk perception and decision making; indoor air pollution; risk communication; ground water and soil pollution modeling and monitoring.

Most Relevant Publications

Small, M.J. 1997. Groundwater detection monitoring using combined information from multiple constituents.

Water Resources Research, 33(5): 957-969.
Casman, E.A., B. Fischhoff, C. Palmgren, M.J. Small and F. Wu. 2000. An integrated risk model of a drinking-water-borne cryptosporidiosis outbreak. *Risk Analysis*, 20(4): 495-511.
Gurian, P.L, M.J. Small, J.R. Lockwood III and M.J. Schervish. Benefit-cost estimation for alternative drinking water maximum contaminant levels. *Water Resources Research*, 37(9): 2213-2226.
Lockwood, J.R., M.J. Schervish, P. Gurian and M.J. Small. 2001. Characterization of arsenic occurrence in source waters of US community water systems. *Journal of the American Statistical Association*, 96(456): 1184-1193.
Gurian, P.L, M.J. Small, J.R. Lockwood III and M.J. Schervish. 2001. Addressing uncertainty and conflicting cost estimates in revising the arsenic MCL. *Environmental Science & Technology*, 35(22): 4414-4420.
Gurian, P.L. and M.J. Small. 2002. Point-of-use treatment and the revised arsenic MCL. *Journal* American Water Works Association, 94(3): 101-108.
DeKay, M.L., M.J. Small, P.S. Fischbeck, R.S. Farrow, A. Cullen, J.B. Kadane, L. Lave, M.G. Morgan and K. Takemura. 2002. Risk-based decision analysis in support of precautionary policies. *Journal of Risk Research*, 5(4): 391-417.
Ailamaki, A., C Faloutsos, P.S. Fischbeck, M.J. Small, J. VanBriesen. 2003. An environmental sensor network to determine drinking water quality and security. *SIGMOD Record*, 32(4): 47-52.
Gurian, P.L, M.J. Small, J.R. Lockwood and M.J. Schervish. 2004. Benefit-cost implications of multicontaminant drinking water standards. *Journal American Water Works Association*, 96(3): 70-83.
Lockwood, J.R., M.J. Schervish, P. Gurian and M.J. Small. 2004. Analysis of contaminant co-occurrence in community water systems. *Journal of the American Statistical Association*, 99(465): 45-56.
McDaniels, T.L. and M.J. Small. 2004. *Risk Analysis and Society: An Interdisciplinary Characterization of the Field*. Cambridge University Press, Cambridge, UK.

Other Significant Publications

Merz, J., M.J. Small and P. Fischbeck. 1992. Measuring decision sensitivity: A combined Monte Carlo-logistic regression approach. *Medical Decision Making*, 12: 189-196.
Crawford, S.L., M.H. DeGroot, J.B. Kadane and M.J. Small. 1992. Modeling lake-chemistry distributions: Approximate Bayesian methods for estimating a finite-mixture model. *Technometrics*, 34(4): 441-453.
Wilkes, C.R., M.J. Small, J.B. Andelman, N.J. Giardino and J. Marshall. 1992. Inhalation exposure model for volatile chemicals from indoor uses of water. *Atmospheric Environment*, 26A: 2227-2236.
Ramaswami, A. and M.J. Small. 1994. Modeling the spatial variability of natural trace element concentrations in groundwater. *Water Resources Research,* 30: 269-282.
Dakins, M.E., J.E. Toll and M.J. Small. 1994. Risk-based environmental remediation: Decision framework and role of uncertainty. *Environmental Toxicology & Chemistry*, 13: 907-1915.
Brand, K. P. and M.J. Small. 1995. Updating uncertainty in an integrated risk assessment: Mathematical framework and methods, *Risk Analysis*, 15(6): 719-731.
Dakins, M.E., J.E. Toll. M.J. Small and K.P. Brand. 1996. Risk-based environmental remediation: Bayesian Monte Carlo analysis and the expected value of sample information. *Risk Analysis,* 16(1): 67-79.
Stiber, N.A., M. Pantazidou and M.J. Small. 1999. Expert system methodology for evaluating reductive dechlorination at TCE sites. *Environmental Science & Technology*, 33(17): 3012-3020.
Sohn, M.D., M.J. Small and M. Pantazidou. 2000. Reducing uncertainty in groundwater site characterization using Bayes Monte Carlo methods. *Journal of Environmental Engineering*, 126(10): 893-902.
Riley, D.M., B. Fischhoff, M.J. Small and P. Fischbeck. 2001.Evaluating the effectiveness of risk-reduction strategies for consumer chemical products. *Risk Analysis*, 21, 357-369.
Kovacs, D.C., B. Fischhoff and M.J. Small. 2001. Perceptions of PCE use by dry cleaners and dry cleaning customers. *Journal of Risk Research*, 4(4): 353-375.
Yeh, S. and M.J. Small. 2002. Incorporating exposure models in probabilistic assessment of the risks of premature mortality from particulate matter. *Journal of Exposure Analysis and Environmental Epidemiology*, 12: 389-403.
Frey, H.C. and M.J. Small. 2003. Integrated environmental assessment, Part 1: Estimating emissions. *Journal of Industrial Ecology*, 7(1): 9-11.
Schultz, M.T., M.J. Small, R.S. Farrow and P.S. Fischbeck. 2004 State water pollution control policy insights from a reduced-form model. *Journal of Water Resources Planning and Management*, 130(2): 150-159.

Current and Pending Support

(See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Mitchell J. Small	Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Effects of Sediment Biogeochemistry on the Environmental Fate and Persistence of Polychlorinated Biphenyls (PCBs)

Source of Support: David and Lucile Packard Foundation

Total Award Amount: $1,000,000 Total Award Period Covered: 07/01/2001 – 8/31/2005

Location of Project: Pittsburgh, PA

Person-Months Per Year Committed to the Project. Cal: Acad: 0.5 mm/yr Summ: 0.5 mm/yr

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Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Consortium for Atlantic Regional Assessment (CARA)

Source of Support: U.S. Environmental Protection Agency ,ORD (Subcontract to Penn State University)

Total Award Amount: $1,250,000 ($300,000 subcontract to CMU) Total Award Period Covered: 9/01/02 – 8/31/05

Location of Project: Pittsburgh, PA

Person-Months Per Year Committed to the Project. Cal: Acad: 0.2 mm/yr Summ: 0.25 mm/yr

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Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: SENSORS: Placement and Operation of an Environmental Sensor Network to Facilitate Decision Making Regarding Drinking Water Quality and Security

Source of Support: National Science Foundation

Total Award Amount: $1,500,000 Total Award Period Covered: 9/03 – 8/06

Location of Project: Pittsburgh, PA

Person-Months Per Year Committed to the Project. Cal: Acad: 0.5 mm/yr Summ: 0.5 mm/yr

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Support: ■ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Tracking Heavy Metal Life Cycle Pathways with Input-Output Methods

Source of Support: National Science Foundation

Total Award Amount: $1,190,000 Total Award Period Covered: 9/03 – 8/06

Location of Project: Pittsburgh, PA

Person-Months Per Year Committed to the Project. Cal: Acad: 0.33 mm/yr Summ: 0.33 mm/yr

Support: ☐ Current ■ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support	
Project/Proposal Title: Air Toxics in Allegheny County: Sources, Airborne Concentrations, and Human Exposure	
Source of Support: Allegheny County Health Department	
Total Award Amount: $600,000	Total Award Period Covered: 1/05 – 12/06
Location of Project: Pittsburgh, PA	
Person-Months Per Year Committed to the Project.	Cal: Acad: 0.5 mm/yr Summ: 0.25 mm/yr

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

BIOGRAPHICAL SKETCH

NAME:	POSITION TITLE
Ewen C.D. Todd	Director, National Food Safety and Toxicology Center

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Glasgow	B.Sc.	1963	Bacteriology
University of Glasgow	Ph.D.	1968	Taxonomy of Staphylococci and Micrococci

Positions and Honors:

2001-Present Director, National Food Safety and Toxicology Center, Michigan State University

1971-2001 Head, Methodology/Contaminated Foods Section, Bureau of Microbial Hazards, Health Protection Branch, Health Canada, Ottawa, Canada.

1976-2001 Chairman, Foodborne Disease Reporting Centre, Bureau of Microbial Hazards, Health Protection Branch, Health Canada, Ottawa, Canada.

1976-2001 Co-chairman, Botulism Reference Centre, Bureau of Microbial Hazards, Health Protection Branch, Health Canada, Ottawa, Canada.

1968-2001 Joint Chief of the Research Division (with Jeff Farber), Bureau of Microbial Hazards, Health Protection Branch, Health Canada, Ottawa, Canada.

Awards:

1992 Citation Award from the International Association of Milk, Food and Environmental Sanitarians for many years of devotion to the ideals of the Association.

1997 Distinctive Service Award for extraordinary teamwork and support to the Science and Technology Community (management of human resources in the Canadian federal government science departments) August 29, 1997, Ottawa.

1999 Recipient of the Excellence in Science Award for 1998, the first to be awarded by Health Canada, March 23, Ottawa

1999 Deputy Minister's Award of Team Excellence in 1999 for the work done in promoting the Fight BAC! campaign in Canada, June 15, Ottawa.

2001 International Association for Food Protection Fellows Award (Minneapolis, August, 2001).

2001 Professional Institute of the Public Service of Canada Gold Medal for Pure and Applied Science (Ottawa, July 2001) [given to one government scientist every two years].

Selected Appointments (last 5 years):

1999 Recipient of the Excellence in Science Award for 1998, the first to be awarded by Health Canada, March 23, Ottawa

1999 Deputy Minister's Award of Team Excellence in 1999 for the work done in promoting the Fight BAC! campaign in Canada, June 15, Ottawa.

2001 International Association for Food Protection Fellows Award (Minneapolis, August, 2001).

2001 Professional Institute of the Public Service of Canada Gold Medal for Pure and Applied Science (Ottawa, July 2001). (awarded to one scientist in a government department every second year; there were 15 applicants in 2001)

1977-01 Literature citations: from 1974 to July, 2001 there were 1563 citations of works by E.C.D. Todd. Seven were cited 40 or more times, and an additional 3 over 100 times, including: Preliminary estimates of costs of foodborne disease in the United States (J. Food Prot. 52: 595-601, 1989); Bates et al: Pennate diatom Nitzschia pungens as a primary source of domoic acid, a toxin in shellfish from eastern Prince Edward, Canada (Can. J. Fish Aquat. Sci.

46: 1203).

2003-present Improving Fish Advisory Awareness in the Upper Peninsula of Michigan Steering Committee

2004-present MSU University Outreach & Engagement Directors' Advisory Team

Publications (last 4 years):

Todd, E. C. D., Szabo, R. A., Mackenzie, J. M., Martin, A., Sandhu, K., Rahn, K., Gyles, C., Alves, D. and Yee, A. **1999**. J. Application of a DNA hybridization-hydrophobic grid membrane filter method for detection of verotoxigenic Escherichia coli. Appl. Environ. Microbiol. 65: 4775-4780.

Farber, J. and Todd, E. C. D. (eds.). **1999**. Safe Food Handling Marcel Dekker, Inc. New York. pp. 1 – 552.

Sockett, P. and Todd, E. C. D. **2000**. The economic costs of foodborne disease. In Microbiological Safety and Quality of Food. B. M. Lund, T. C. Baird-Parker, and G. W. Gould (eds.). Aspen Publishers, Gaithersburg, MD. pp. 1563-1588.

Todd, E.C.D. **2001**. Surveillance of foodborne disease. In Foodborne Disease Handbook: Diseases Caused by Bacteria, Hui, Y.H., M. D. Pierson, and J. R. Gorham. (eds.) 2nd edition. Marcel Dekker, Inc., New York, pp. 515 - 585.

Bisaillon, J.-R., Feltmate, T.E., Sheffeld, S., Julian, R., Todd, E.C.D., Poppe, C., and Quessy, S. **2001**. Classification of grossly etectable abnormalities and conditions seen at post-mortem in Canadian Poultry abattoirs according to a hazard identification decision tree. J. Food Protection 64: 1973-1980.

Banerjee, S.K., Pandian, S., Todd, E.C.D., and Farber, J.M. **2002**. A rapid and improved method for the detection of Vibrio parahaemolyticus and Vibrio vulnificus strains grown on hydrophobic grid membrane filters. J. Food Protection 65: 1049-1053.

Todd, E. Contamination of food. In Encyclopaedia of Food Sciences and Nutrition. **2003**. Caballero, B., Trugo, L, and Finglas, P. (eds). Academic Press, London, UK. pp. 1593-1600.

Todd, E.C. D. **2003**. Microbiological safety standards and public health goals to reduce foodborne disease. Meat Science 66:33-43.

Duff, Steven, Scott, Elizabeth, Mafilios, Michael, Todd, Ewen C., Krilov, Leonard, Geddes, Alasdair, and Ackerman, Stacey J. **2003**. Cost-effectiveness of a targeted disinfection program in household kitchens to prevent foodborne illnesses in the United States, Canada, and the United Kingdom. J. Food Protection 66 (11): 2103-2115.

Todd, E. C. D., **2004**. Risk management – a glimpse forward. In Pre-Harvest and Post-Harvest Food Safety: Contemporary Issues and Future Directions. Ross C. Beier, Suresh D. Pillai, Timothy D. Phillips, Richard L. Ziprin (Eds.), Iowa State Press, a Blackwell Publishing Company, Ames, IA.

Michaels, B., Keller, C., Blevins, M., Paoli, G., Todd, E., and Griffith C.J. **2004**. Use of quantitative microbial risk assessment approaches for determination of effective hygiene interventions to prevent food handler transmission of foodborne pathogens. Food Service Technology (in press).

FAO/WHO. **2004**. Authors: Buchanan, R., Lindqvist, R., Ross, T., Smith, M., Todd, E., and Whiting, R. Risk assessment of Listeria monocytogenes in ready-to-eat foods: Technical Report. FAO/WHO Microbiological Risk Assessment Series, No.5. pp. 1-307.

Lammerding, A. M., and Todd, E.C.D. **2004**. Microbial food safety risk assessment. In Foodborne Infections and Intoxications, 3rd edition, D. Cliver and H. Riemann (eds.), Academic Press (in press).

Expert Scientific Review Panel on Listeria Monocytogenes in Foods (E. Todd, member) **2004**. Report. Achieving Continuous Improvement In Reductions In Listeriosis - A Risk Based Approach, International Life Sciences Institute, Washington, DC.

Rooney, R., Bartram, J., Cramer, E., Mantra, S., Nichols, G., Farber, J., Todd, E., Forney, D., Harper, D., Suraj, R. **2004**. Water safety on ships: a review of outbreaks from waterborne disease from January 1970 to June 2003. Public Health Record (in press).

Rooney, R., Cramer, E., Mantra, S., Bartram, J., Nichols, G., Farber, J., Todd, E., Forney, D., Harper, Ben Embarek, P., D., Suraj, R. **2004**. Food safety on ships: a review of outbreaks from foodborne disease from January 1970 to June 2003. Public Health Record (in press).

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Ewen Todd

Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
Transfer Coefficients for Listeria Cross-Contamination

Source of Support: Food and Drug Administration
Total Award Amount: $ 583,087 Total Award Period Covered: 9/30/2001-9/29/2004
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 2 Acad: Sumr:

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
Microbial reduction strategies for Highbush Blueberries

Source of Support: U.S. Highbush Blueberry Council
Total Award Amount: $90,459 Total Award Period Covered: 5/1/2003 - 4/30/2005
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 4 Acad: Sumr:

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
Microbial standards and reduction strategies for Highbush blueberries

Source of Support: Midwest Advance Food Mfg Alliance (MAFMA)
Total Award Amount: $50,000 Total Award Period Covered: 8/1/2003 - 5/31/2005
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 4 Acad: Sumr:

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
Conductometric biosensor for foodborne pathogen detection in fresh produce

Source of Support: U.S. Department of Ag (USDA)/CSREES
Total Award Amount: $295,790 Total Award Period Covered: : 9/1/2003 - 8/31/2005
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 3 Acad: Sumr:

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
Transfer rates for listeria monocytogenes during retail slicing and handling of delicatessen ham

Source of Support: U.S. Department of Ag (USDA)
Total Award Amount: $ 136,872 Total Award Period Covered: 10/1/2003 - 9/30/2005
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 2 Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Ewen Todd (cont.)

Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
Addressing food safety and marketing concerns through microbial reduction strategie for Michigan Blueberries

Source of Support: MI Agriculture
Total Award Amount: $89,530 Total Award Period Covered: 1/1/2003 - 12/31/2005
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 4 Acad: Sumr:

Support: [x] Current [ ] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
Food Safety Policy Center REF

Source of Support: MSU Office of the Vice President for Research & Graduate Studies
Total Award Amount: $300,000 Total Award Period Covered: 1/7/2004 - 6/30/2009
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 11 Acad: Sumr:

Support: [ ] Current [x] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
DETERMINATION OF BEST CONSUMED BY TIMES FOR LISTERIA MONOCYTOGENES IN READY-TO-EAT MEATS

Source of Support: U.S. Department of Ag (USDA)
Total Award Amount: $220,000 Total Award Period Covered: 9/1/2004 - 8/31/2006
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 3 Acad: Sumr:

Support: [ ] Current [x] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
PREDICTIVE MODELS FOR MINIMIZING LISTERIA TRANSFER DURING SLICING OF DELICATESSEN MEATS

Source of Support: US DEPT OF AG- USDA
Total Award Amount: $499,982 Total Award Period Covered: 10/1/2004 - 9/30/2007
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 4 Acad: Sumr:

Support: [ ] Current [x] Pending [ ] Submission Planned in Near Future [ ] *Transfer of Support
Project/Proposal Title:
USE OF A BIOSENSOR FOR MONITORING PATHOGEN TRANSMISSION IN FRESH PRODUCE

Source of Support: US DEPT OF AG- USDA
Total Award Amount: $100,000 Total Award Period Covered: 1/1/2005 - 12/31/2007
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 3 Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Ewen Todd (cont.)	Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title:
THE ROLE OF THIRD PARTY CERTIFICATION FOR FOOD SAFETY IN CHINA

Source of Support: USDA - FOREIGN AG SER
Total Award Amount: $45,000 Total Award Period Covered: 7/1/2004 - 6/30/2006
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 4 Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title:
EARLY CBRN ATTACK DETECTION BY COMPUTERIZED MEDICAL RECORD SURVEILLANCE

Source of Support: Canadian Department of National Defense CRTI
Total Award Amount: $92,946 Total Award Period Covered: : 10/1/2004 - 9/30/2006
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 2 Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title:
RAPID PATHOGEN SCREENING TO MINIMIZE EXPOSURE TO E COLI O157:H7 IN BEEF CATTLE PRODUCTION

Source of Support: U.S. Department of Ag (USDA)
Total Award Amount: $477,100 Total Award Period Covered: : 7/1/2004 - 6/30/2007
Location of Project: MSU
Person-Months Per Year Committed to the Project. Cal: 3 Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

NCER FORM 5 (9/01) For Use with EPA STAR Grant Applications

USE ADDITIONAL SHEETS AS NECESSARY

Rosina Weber

College of Information Science and Technology, Drexel University
Phone: +1 215 895 1911 E-mail: Rosina.Weber@drexel.edu

Professional Preparation :

Federal University of Rio Grande do Sul, Brazil: Bachelors in Business Administration; 1988
Federal University of Santa Catarina, Brazil: M.Sc.; 1993
Federal University of Santa Catarina, Brazil: Doctorate; 1998

Appointments:

Aug, 2001 to present: Assistant Professor; College of Information Science and Technology; Drexel University, Philadelphia, PA
Sep, 1999 to Aug, 2001: Post Doc; Navy Center for Applied Research in Artificial Intelligence; Naval Research Laboratory, Washington, DC
Jan to Sep,1999: Adjunct Professor; College of Business, at the Center for Education- UNICA, SC, Brazil.
Sep, 1998 to Aug, 1999: Assistant Professor; College of Business, Social Sciences, and Economics at Brazilian Lutheran University, RS, Brazil.
Aug, 1994 to May, 1998: Research assistant; Department of Production Engineering at Federal University of Santa Catarina, Brazil.
Mar, 1996 to May, 1998: Lecturer; Department of Production Engineering at Federal University of Santa Catarina, Brazil.
Jan, 1986 to Jul, 1989: Multiple positions in industry mainly in the Finance, in Brazil.

Publications:

Five Relevant Publications:

1. Weber, R., Evanco, W., Waller, M., Verner, J. (2004). Identifying Critical Factors in Case-Based Prediction.. In Valerie Barr and Zdravko Markov (eds.) Proceedings of the Seventeenth Annual Conference of the International Florida Artificial Intelligence Research Society, 207-212. Menlo Park, CA: AAAI Press.
2. Weber, R. & Aha, D.W. (2003). Intelligent delivery of military lessons learned. Decision support systems 34, 3, 287-304.
3. Weber, R. & Kaplan, R. (2003). Knowledge-based knowledge management. Innovations in Knowledge Engineering. Ravi Jain, Ajith Abraham, Colette Faucher and Berend Jan van der Zwaag (eds.). Adelaide:Advanced Knowledge International Pty Ltd.
4. Weber, R., Aha, D.W., & Becerra-Fernandez, I. (2001). Intelligent lessons learned systems. International Journal of Expert Systems Research & Applications, 20, 1, 17-34.
5. Aha, D.W., Weber, R., Muñoz, H., Breslow, L.A. & Gupta, K. (2001). Bridging the Lesson Distribution Gap. Proceedings of IJCAI'01 (Seattle, WA, Aug 2001), Seattle, WA: Morgan Kaufmann Publishers, 987-992. http://www.pages.drexel.edu/~rw37/publications.html

Five Other Publications:

6. Weber, R., Wu, D. (2004). Knowledge Management for Computational Intelligence Systems. Eighth IEEE International Symposium on High Assurance Systems Engineering (HASE 2004), 116-125. IEEE Computer Society:Los Alamitos, CA.

7. Weber, R., Waller, M., Verner, J., Evanco, B. (2003). Predicting Software Development Project Outcomes. In D. Bridge and K. Ashley (eds.) Case-Based Reasoning Research and Development. LNAI 2689, 595-609. Berlin Heidelberg:Springer-Verlag.
8. Weber, R., Sandhu, N., & Breslow, L. (2001). Weber, R., Breslow, L., Sandhu, N. (2001).

On the Technological, Human, and Managerial Issues in Sharing Organizational Lessons. In Proceedings of the Fourteenth Annual Conference of the International Florida Artificial Intelligence Research Society, 334-338. Menlo Park, CA: AAAI Press.
9. Weber, R. & Aha, D.W. (2002). Intelligent Elicitation of Military Lessons. In Proceedings of the Sixth International Conference on Intelligent User Interfaces, San Francisco, CA, January 14-17, 2002.
10. Weber, R., Aha, D.W., Muñoz-Avila, H., & Breslow, L.A. (2000). An Intelligent lessons learned process. Z.W. Rás & S. Ohsuga (Eds.):ISMIS, LNAI 1932, 358-367. Berlin:Springer-Verlag.

Synergistic Activities:

1. Member of editorial board of the International Journal on Knowledge-Based Intelligent Engineering Systems and the International Journal of Hybrid Intelligent Systems. Invited reviewer for Decision Support Systems, the International Journal of Smart Engineering System Design, Applied Intelligence, European Journal of Information Systems, IEEE Intelligent Systems & their Applications, and the German Journal on Artificial Intelligence. Reviewer of knowledge management related conferences such as PAKM, CIKM, IJCAI, ICCBR, FLAIRS, ICIS, ECAI, WM.
2. Surveyed lessons-learned systems.
3. Developed methodologies for textual CBR for active delivery of lessons-learned.
4. Co-organization of the AAAI Workshop on Intelligent Lessons Learned Systems in 2000, http://www.aaai.org/Press/Reports/Workshops/ws-00-03.html. Co-organization of the Workshop Program at the International Conference on CBR 2001. Chair of the CBR Special Track - FLAIRS 2001.

Collaborators & Other Affiliations:

(a) Collaborators and Co-Editors:
Aha, David W. - Navy Center for Applied Research in Artificial Intelligence, Naval Research Laboratory, USA; Becerra-Fernandez, Irma - Florida International University, USA; Branting, L.K. - LiveWire Logic, Inc., Raleigh, NC; Breslow, Len - Navy Center for Applied Research in Artificial Intelligence, Naval Research Laboratory, USA; Evanco, William - Drexel University, USA; Gupta, Kalyan - ITT Industries, USA; Kaplan, Randy - Drexel University, USA; Lucas, John Robert - Joint Center for Lessons Learned/USJFCOM, Joint Warfighting Center, USA; Munoz-Avila, Hector - Lehigh University, USA; Nau, Dana - University of Maryland, USA; Sandhu, Nabil - ITT Industries, USA; Verner, June - Drexel University, USA; Yamal, Fusun - University of Maryland, USA;

Graduate and Postdoctoral Advisors.

Barcia, Ricardo M. – Federal University of Santa Catarina, Brazil; Aha, David W. (above)

Graduate Students:

Proctor, Jason M.; Fowler, Caleb

Current and Pending Support

(See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: **Rosina Weber**

Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **CAREER: Apprentice Methods**

Source of Support: **NSF**

Total Award Amount: $ **500,586** Total Award Period Covered: **04/01/05 - 03/31/10**

Location of Project: **Drexel University**

Person-Months Per Year Committed to the Project. Cal: **0.00** Acad: **0.00** Sumr: **1.79**

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: **Case Based Reasoning for Software Testing**

Source of Support: **Dept. of Navy via University of Southern Florida**

Total Award Amount: $ **172,130** Total Award Period Covered: **12/01/02 - 09/30/04**

Location of Project: **Drexe l University**

Person-Months Per Year Committed to the Project. Cal: **0.00** Acad: **2.89** Sumr: **0.32**

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Summ:

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*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

USE ADDITIONAL SHEETS AS NECESSARY

Project **Center for Advancing Microbial Risk Assessment**
PI **Joan Rose**
Institution **Michigan State University**
Indirect Cost Rates **51.0% (Year 1) 51.0% (Years 2-5)**
Project Dates 5/16/05 to 5/15/10

		Year 1 - Rose				Year 2 - Rose				Year 3 - Rose			
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Federal Total
Dr. Syed Hashsham--SU (3 months)	1	100.0%	$26,140	$2,000	$28,139	100.0%	$27,447	$2,100	$29,546	100.0%	$28,819	$2,205	$31,024
Staff 1	1	100.0%	$40,750	$18,460	$59,210	100.0%	$41,973	$19,727	$61,700	100.0%	$43,232	$21,011	$64,242
Post-doctoral Associates													
Post-Doc 1	1	100.0%	$45,844	$12,240	$58,084	100.0%	$47,219	$13,174	$60,394	100.0%	$48,636	$14,104	$62,740
Post-Doc 2	1	100.0%	$45,844	$12,240	$58,084	100.0%	$47,219	$13,174	$60,394	100.0%	$48,636	$14,104	$62,740
Graduate Assistants													
Level I, 1/2 time	2	100.0%	$49,992	$2,908	$52,900	100.0%	$51,492	$3,084	$54,576	100.0%	$54,230	$3,268	$57,498
Total Personnel			**$208,569**	**$47,848**	**$256,417**		**$215,350**	**$51,259**	**$266,609**		**$223,553**	**$54,692**	**$278,243**
Travel & Meetings		Travel	Meetings	Other		Travel	Meetings	Other		Travel	Meetings	Other	
Domestic (30 trips at $2000/trip 1st year)		$60,000			$60,000	$60,000			$60,000	$60,000			$60,000
Total Travel					**$60,000**				**$60,000**				**$60,000**
Equipment (detail)													
Total Equipment					**$0**								**$0**
Supplies & Services (by category)													
Biochip fabrication					$30,000				$30,000				$45,000
Water sample processing					$1,000				$7,500				$20,000
Animal zoonoses experiments					$10,000				$40,000				$40,000
Computer costs					$3,000								
Axon Scanner user fee					$5,000				$5,000				$5,000
Total Supplies & Services					**$49,000**				**$82,500**				**$110,000**
Other (detail)													
Other (detail)					$12,903				$15,228				$5,000
Tuition (grad students; no overhead)					$11,276				$15,228				$16,448
Total Other					**$24,179**				**$30,456**				**$21,448**
Subcontracts													
University of Arizona					203,254				$193,351				$200,682
University of Michigan					149,997				$164,999				$170,000
Northern Arizona University					101,439				$103,609				$105,844
Drexel University					454,326				$458,228				$439,893
University of California Berkeley					307,069				$322,424				$338,544
Carnagie Mellon					95,709				$101,009				$40,665
Total Subcontracts					$1,311,794				$1,343,620				$1,295,628
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)					150000								
Total Direct Costs					$1,701,390				$1,783,184				$1,765,319
Indirect Costs					$269,443				$216,412				$231,154
Total Costs					$1,970,833				$1,999,596				$1,996,472

Project	**Center for Advancing Microbial Risk Assessment**
PI	**Joan Rose**
Institution	**Michigan State University**
Indirect Cost Rates	**51.0% (Year 1) 51.0% (Years 2-5)**
Project Dates	5/16/05 to 5/15/10

		Year 4 - Rose				Year 5 - Rose				Yrs 1-5
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Federal Total	**Project Total**
Dr. Syed Hashsham--SU (3 months)	1	100.0%	$30,260	$2,315	$32,575	100.0%	$31,773	$2,431	$34,204	$155,488
Staff 1	1	100.0%	$44,529	$22,398	$66,927	100.0%	$45,864	$23,758	$69,622	$321,700
Post-doctoral Associates										
Post-Doc 1	1	100.0%	$50,095	$23,494	$73,589	100.0%	$51,598	$24,870	$76,468	$331,274
Post-Doc 2	1	100.0%	$50,095	$23,494	$73,589	100.0%	$51,598	$24,870	$76,468	$331,274
Graduate Assistants										
Level I, 1/2 time	2	100.0%	$55,857	$3,464	$59,321	100.0%	$57,532	$3,672	$61,204	$285,499
Total Personnel			**$230,836**	**$75,166**	**$306,000**		**$238,366**	**$79,600**	**$317,964**	$1,425,233
Travel & Meetings		Travel	Meetings	Other		Travel	Meetings	Other		
Domestic (30 trips at $2000/trip 1st year)		$60,000			$60,000	$60,000			$60,000	
Total Travel					**$60,000**				**$60,000**	$300,000
Equipment (detail)										
Total Equipment					**$0**				**$0**	$0
Supplies & Services (by category)										
Biochip fabrication					$30,000				$12,000	
Water sample processing					$20,000				$20,000	
Animal zoonoses experiments					$40,000				$12,000	
Computer costs										
Axon Scanner user fee					$5,000					
Total Supplies & Services					**$95,000**				**$44,000**	$380,500
Other (detail)										
Other (detail)					$5,000				$5,000	
Tuition (grad students; no overhead)					$17,764				$19,184	
Total Other					**$22,764**				**$24,184**	$123,031
Subcontracts										
University of Arizona					$206,561				$211,060	$1,014,908
University of Michigan					$174,981				$184,996	$844,973
Northern Arizona University					$108,145				$110,516	$529,553
Drexel University					$413,705				$437,600	$2,203,752
University of California Berkeley					$355,471				$373,246	$1,696,753
Carnagie Mellon					$16,705				$17,272	$271,360
Total Subcontracts					$1,275,568				$1,334,690	$6,561,299
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)										
Total Direct Costs					$1,759,332				$1,780,838	$8,790,063
Indirect Costs					$237,660				$217,752	$1,172,421
Total Costs					$1,996,993				$1,998,590	**$9,962,484**

Project Center for Assessment of Microbial Risk Agents
PI Dr. Charles N. Haas
Institution Drexel University
Indirect Cost Rates 50.0% (Year 1) 50.0% (Years 2-5)
Project Dates 5/16/05 to 5/15/10

		Year 1 - Haas					Year 2 - Haas					Year 3 - Haas			
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	Year 1 Cost Share	% Effort	Budgeted Salary	Budgeted Fringes	Total	Year 2 Cost Share	% Effort	Budgeted Salary	Budgeted Fringes	Total
Haas, Charles (Summer)	1	28.5%	$18,810	$4,477	$23,287		28.5%	$19,751	$4,701	$24,452		28.5%	$20,738	$4,936	$25,674
Haas, Charles (AY Time)	1	11.9%	$19,594	$4,663	$24,257		11.9%	$20,573	$4,896	$25,470		11.9%	$11,602	$2,761	$14,363
Gurian, Patrick (Summer)	1	8.4%	$3,000	$714	$3,714		8.4%	$3,150	$750	$3,900		8.4%	$3,308	$787	$4,095
Gurian, Patrick (AY time)	1	18.0%	$16,051	$3,820	$19,871		8.6%	$7,640	$1,818	$9,458		8.0%	$7,532	$1,793	$9,325
Weber, Rosina (Summer)	1	7.5%	$2,400	$571	$2,971		46.5%	$15,500	$3,689	$19,189		9.1%	$3,200	$762	$3,962
Weber, Rosina (AY time)	1	21.8%	$17,334	$4,126	$21,460		21.8%	$18,201	$4,332	$22,533					
Atwood, Michael	1	26.7%	$13,000	$3,094	$16,093		0.0%	$0	$0	$0		0.0%		$0	$0
Han, Hyoil	1	0.0%		$0	$0		0.0%	$0	$0	$0		8.9%	$8,820	$2,099	$10,920
Project Coordinator	1	67.0%	$26,800	$6,378	$33,178		67.0%	$28,140	$6,697	$34,837		67.0%	$29,547	$7,032	$36,579
Programmer 1 (PHP Programmer)	1	100.0%	$22,693	$5,401	$28,094		100.0%	$10,178	$2,422	$12,600		0.0%	$0		$0
Programmer 2 (Oracle Programmer)	1	0.0%		$0	$0		0.0%		$0	$0		100.0%	$20,186	$4,804	$24,990
	1														
Post-doctoral Researchers															
Post-doc	0														
Research Assitants															
Graduate student	5	100.0%	$70,500		$70,500		100.0%	$95,025		$95,025		100.0%	$99,777		$99,777
Undergrad hourly	1	100.0%													
Total Personnel			**$210,181**	**$33,244**	**$243,425**			**$218,158**	**$29,306**	**$247,464**			**$204,710**	**$24,974**	**$229,685**
Travel & Meetings															
Domestic- Scientific & CAMRA meetings					$11,500					$12,700					$6,700
Foreign															
Total Travel					**$11,500**					**$12,700**					**$6,700**
Equipment (detail)															
Total Equipment					**$0**					**$0**					**$0**
Supplies & Services (by category)															
(Provide major categories, add lines as needed)															
Computers					$6,481										$4,096
Misc. supplies, incl. data storage devices, computer software, and upgrades					$3,751					$5,709					$5,150
Total Supplies & Services					**$10,232**					**$5,709**					**$9,246**
Other (detail)															
Publication costs															
Graduate tuition					$56,590	$43,170				$59,420	$69,122				$71,447
Total Other					**$56,590**					**$59,420**					**$71,447**
Subcontracts															
Total Subcontracts															
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)															
Total Direct Costs					$321,747	$43,170				$325,292	$69,122				$317,077
Indirect Costs					$132,579	$0				$132,936	$0				$122,815
Total Costs					$454,326	$43,170				$458,228	$69,122				$439,893

Project **Center**
PI **Haas**
Institution **Drexel**
Indirect Cost Rates
Project Dates

		Year 4 - Haas					Year 5 - Haas					Yr 1-5	Yr 1-5
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	Year 4 Cost Share	% Effort	Budgeted Salary	Budgeted Fringes	Total	Year 5 Cost Share	**Cumulative Total**	**Total Cost Share**
Haas, Charles (Summer)	1	24.1%	$17,541	$4,175	$21,716		24.1%	$18,418	$4,383	$22,801		$117,929	$0
Haas, Charles (AY Time)	1	11.9%	$22,682	$5,398	$28,081		11.9%	$23,816	$5,668	$29,485		$121,655	$12,380
Gurian, Patrick (Summer)	1	8.4%	$3,473	$827	$4,300		10.8%	$4,445	$1,058	$5,503		$21,511	$0
Gurian, Patrick (AY time)	1	3.1%	$3,065	$729	$3,794		0.0%		$0	$0		$42,448	$0
Weber, Rosina (Summer)	1	5.4%	$2,000	$476	$2,476		18.7%	$7,200	$1,714	$8,914		$37,511	$0
Weber, Rosina (AY time)	1	25.2%	$23,152	$5,510	$28,662		21.8%	$21,069	$5,014	$26,083		$98,738	$0
Atwood, Michael	1	0.0%		$0	$0		0.0%		$0	$0		$16,093	$0
Han, Hyoil	1	8.9%	$9,261	$2,204	$11,466		0.0%		$0	$0		$22,385	$0
Project Coordinator	1	67.0%	$31,024	$7,384	$38,408		67.0%	$32,576	$7,753	$40,329		$183,331	$0
Programmer 1 (PHP Programmer)	1			$0	$0				$0	$0		$40,694	$0
Programmer 2 (Oracle Programmer)	1			$0	$0				$0	$0		$24,990	$0
	1												
Post-doctoral Researchers													
Post-doc	0											$0	$0
Research Assitants													
Graduate student	5	100.0%	$81,614		$81,614		100.0%	$85,695		$85,695		$432,611	$0
Undergrad hourly	1						100.0%	$12,000		$12,000		$12,000	$0
												$1,171,899	$12,380
Total Personnel			**$193,812**	**$26,703**	**$220,516**			**$205,219**	**$25,591**	**$230,810**		**$1,171,899**	**$12,380**
Travel & Meetings													
Domestic- Scientific & CAMRA meetings					$6,261					$6,800		$43,961	$0
Foreign												$0	$0
Total Travel					**$6,261**					**$6,800**		**$43,961**	**$0**
Equipment (detail)													
Total Equipment					**$0**					**$0**		**0**	**0**
Supplies & Services (by category)													
(Provide major categories, add lines as needed)													
Computers					$3,500							$14,077	$0
Misc. supplies, incl. data storage devices, computer software, and upgrades					$7,853					$7,766		$30,229	$0
Total Supplies & Services					**$11,353**					**$7,766**		**$44,306**	**$0**
Other (detail)													
Publication costs										$500		$500	$0
Graduate tuition					$56,511	$33,988				$68,786	$26,237	$312,753	$236,039
Total Other					**$56,511**					**$69,286**		**$313,253**	**$236,039**
Subcontracts													
Total Subcontracts													
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)													
Total Direct Costs					$294,641	$33,988				$314,662	$26,237	**$1,573,419**	**$248,419**
Indirect Costs					$119,065	$0				$122,938	$0	**$630,333**	**$6,190**
Total Costs					$413,705	$33,988				$437,600	$26,237	**$2,203,752**	**$254,609**

Project An EPA/HLS Center of Excellence for Adressing Microbial Risk
PI Dr. Christopher Choi
Institution University of Arizona
Indirect Cost Rates 50.5% (Year 1) 50.5/51% (Year 2) 51.0% (Years 3-5)
Project Dates 5/15/05 to 5/14/10

		Year 1 - PI Name				Year 2 - PI Name				Year 3 - PI Name			
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
Dr. 1													
Dr. 1--SU (3 months)													
Dr. 2													
#REF!													
Post-Doc 1		75.0%	$26,250	$6,828	$33,078	75.0%	$27,038	$7,084	$34,122	75.0%	$27,849	$7,296	$35,145
Post-Doc 2													
Graduate Assistants													
Level I, 1/4 time		25.0%	$10,562	$3,162	$13,724	25.0%	$10,879	$3,351	$14,230	25.0%	$11,205	$3,451	$14,656
Level I, 1/2 time		50.0%	$18,000	$5,389	$23,389	50.0%	$18,540	$5,711	$24,251	50.0%	$19,096	$5,881	$24,977
Level I, 1/2 time		50.0%	$18,000	$5,389	$23,389	50.0%	$18,540	$5,711	$24,251	50.0%	$19,096	$5,881	$24,977
Total Personnel					**$93,580**				**$96,854**				**$99,755**
Travel & Meetings													
Domestic					$4,500				$4,500				$4,500
Foreign													
Total Travel					**$4,500**				**$4,500**				**$4,500**
Equipment (detail)													
Total Equipment													
Supplies & Services (by category)					$40,000				$30,000				$30,000
(Provide major categories, add lines as needed)													
Consultants													
General project supplies, printing, telephone													
Telecommunications													
Total Supplies & Services					**$40,000**				**$30,000**				**$30,000**
Other (detail)													
Publications													$2,000
Total Other					**$0**				**$0**				**$2,000**
Subcontracts													
Total Subcontracts													
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)													
Total Direct Costs					**$138,080**				**$131,354**				**$136,255**
Indirect Costs					**$65,174**				**$61,997**				**$64,427**
Total Costs					**$203,254**				**$193,351**				**$200,682**

Project CAMR
PI Choi
Institution Univer
Indirect Cost Rates
Project Dates

		Year 4 - PI Name				Year 5 - PI Name			
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
Dr. 1									
Dr. 1--SU (3 months)									
Dr. 2									
#REF!									
Post-Doc 1		75.0%	$28,684	$7,515	$36,199	75.0%	$29,545	$7,741	$37,286
Post-Doc 2									
Graduate Assistants									
Level I, 1/4 time		25.0%	$11,541	$3,555	$15,096	25.0%	$11,888	$3,661	$15,549
Level I, 1/2 time		50.0%	$19,669	$6,058	$25,727	50.0%	$20,259	$6,240	$26,499
Level I, 1/2 time		50.0%	$19,669	$6,058	$25,727	50.0%	$20,259	$6,240	$26,499
Total Personnel					**$102,749**				**$105,833**
Travel & Meetings									
Domestic					$4,500				$4,500
Foreign									
Total Travel					**$4,500**				**$4,500**
Equipment (detail)									
Total Equipment									
Supplies & Services (by category)					$30,000				$30,000
(Provide major categories, add lines as needed)									
Consultants									
General project supplies, printing, telephone									
Telecommunications									
Total Supplies & Services					**$30,000**				**$30,000**
Other (detail)									
Publications					$3,000				$3,000
Total Other					**$3,000**				**$3,000**
Subcontracts									
Total Subcontracts									
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)									
Total Direct Costs					**$140,249**				**$143,333**
Indirect Costs					**$66,312**				**$67,727**
Total Costs					**$206,561**				**$211,060**

Project Center for Advancing Microbial Risk Assessment
Principal Investigator Mark Nicas
Institution University of California, Berkeley
Indirect Cost Rates 52.0% (Year 1) 52.0% (Years 2-5)
Project Dates 5/16/05 to 5/15/10

		Year 1 - Nicas, Mark				Year 2 - Nicas, Mark				Year 3 - Nicas, Mark			
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
Dr. Mark Nicas, PI		25.0%	$25,219	$4,287	$29,506	25.0%	$26,480	$4,502	$30,982	25.0%	$27,804	$4,727	$32,531
Dr. Joe Eisenberg, Co-Investigator		25.0%	$19,992	$3,399	$23,391	25.0%	$20,992	$3,569	$24,561	25.0%	$22,042	$3,747	$25,789
Dr. Alan Hubbard, Statistician		10.0%	$6,773	$1,151	$7,924	10.0%	$7,112	$1,209	$8,321	10.0%	$7,468	$1,270	$8,738
Dr. Tom McKone, Risk Analyst		8.3%	$12,053	$2,049	$14,102	8.3%	$12,656	$2,152	$14,808	8.3%	$13,289	$2,259	$15,548
Dr. William Nazaroff, Engineer		8.3%	$12,556	$1,595	$14,151	8.3%	$13,184	$1,674	$14,858	8.3%	$13,843	$1,758	$15,601
Arthur Reingold, MD, Epidemiologist		4.2%	$7,559	$960	$8,519	4.2%	$7,937	$1,008	$8,945	4.2%	$8,334	$1,058	$9,392
Judy Tam, Project Assistant		7.0%	$3,146	$692	$3,838	7.0%	$3,303	$727	$4,030	7.0%	$3,468	$763	$4,231
Graduate Student Researchers													
TBA, GSR II, 9 months		49.9%	$12,034	$241	$12,275	49.9%	$12,636	$253	$12,889	49.9%	$13,268	$265	$13,533
TBA, GSR II, 3 months		100.0%	$8,038	$322	$8,360	100.0%	$8,440	$338	$8,778	100.0%	$8,862	$354	$9,216
TBA, GSR II, 9 months		49.9%	$12,034	$241	$12,275	49.9%	$12,636	$253	$12,889	49.9%	$13,268	$265	$13,533
TBA, GSR II, 3 months		100.0%	$8,038	$322	$8,360	100.0%	$8,440	$338	$8,778	100.0%	$8,862	$354	$9,216
TBA, GSR II, 9 months		49.9%	$12,034	$241	$12,275	49.9%	$12,636	$253	$12,889	49.9%	$13,268	$265	$13,533
TBA, GSR II, 3 months		100.0%	$8,038	$322	$8,360	100.0%	$8,440	$338	$8,778	100.0%	$8,862	$354	$9,216
Total Personnel					**$163,336**				**$171,506**				**$180,077**
Travel & Meetings													
Domestic					$4,000				$4,000				$4,200
Foreign					$0				$0				$0
Total Travel													
Equipment (detail)					$0				$0				$0
Total Equipment													
Supplies & Services (by category)													
Office Supplies					$2,000				$2,000				$2,200
Computers									$3,021				$5,031
Computer Expendables					$1,000				$1,000				$1,000
Printers									$1,000				$0
Laboratory reagents, sample media, glassware					$5,000				$10,000				$10,000
Construction of particle test chamber					$2,500				$0				$0
Air moving fan, sampling pumps					$4,293				$0				$0
Calibration devices					$2,000				$0				$0
Consultants					$0				$0				$0
Telephone and Fax					$1,000				$1,050				$1,103
Photocopying					$700				$735				$772
Total Supplies & Services													
Other (detail)													
Tuition and Fees													
3 GSR In-State Fee Remissions					$24,609				$27,070				$27,882
Total Other													
Subcontracts					$0				$0				$0
Total Subcontracts													
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)													
Total Direct Costs					$210,438				$221,382				$232,265
Indirect Costs					$96,631				$101,042				$106,279
Total Costs					$307,069				$322,424				$338,544

Project	**Center for Advancing Microbial Risk Assessment**
Principal Investigator	**Mark Nicas**
Institution	**University of California, Berkeley**
Indirect Cost Rates	**52.0% (Year 1) 52.0% (Years 2-5)**
Project Dates	**5/16/05 to 5/15/10**

	Year 4 - Nicas, Mark				**Year 5 - Nicas, Mark**			
Personnel: include each person or position on a separate line (add lines as needed)	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
Dr. Mark Nicas, PI	25.0%	$29,194	$4,963	$34,157	25.0%	$30,654	$5,211	$35,865
Dr. Joe Eisenberg, Co-Investigator	25.0%	$23,144	$3,934	$27,078	25.0%	$24,301	$4,131	$28,432
Dr. Alan Hubbard, Statistician	10.0%	$7,841	$1,333	$9,174	10.0%	$8,233	$1,400	$9,633
Dr. Tom McKone, Risk Analyst	8.3%	$13,953	$2,372	$16,325	8.3%	$14,651	$2,491	$17,142
Dr. William Nazaroff, Engineer	8.3%	$14,535	$1,846	$16,381	8.3%	$15,262	$1,938	$17,200
Arthur Reingold, MD, Epidemiologist	4.2%	$8,751	$1,111	$9,862	4.2%	$9,189	$1,167	$10,356
Judy Tam, Project Assistant	7.0%	$3,641	$801	$4,442	7.0%	$3,823	$841	$4,664
Graduate Student Researchers								
TBA, GSR II, 9 months	49.9%	$13,931	$279	$14,210	49.9%	$14,628	$293	$14,921
TBA, GSR II, 3 months	100.0%	$9,305	$372	$9,677	100.0%	$9,770	$391	$10,161
TBA, GSR II, 9 months	49.9%	$13,931	$279	$14,210	49.9%	$14,628	$293	$14,921
TBA, GSR II, 3 months	100.0%	$9,305	$372	$9,677	100.0%	$9,770	$391	$10,161
TBA, GSR II, 9 months	49.9%	$13,931	$279	$14,210	49.9%	$14,628	$293	$14,921
TBA, GSR II, 3 months	100.0%	$9,305	$372	$9,677	100.0%	$9,770	$391	$10,161
Total Personnel				**$189,080**				**$198,538**
Travel & Meetings								
Domestic				$4,200				$4,400
Foreign				$0				$0
Total Travel								
Equipment (detail)				$0				$0
Total Equipment								
Supplies & Services (by category)								
Office Supplies				$2,200				$2,400
Computers				$4,520				$2,690
Computer Expendables				$1,000				$1,000
Printers				$0				$0
Laboratory reagents, sample media, glassware				$12,000				$15,000
Construction of particle test chamber				$0				$0
Air moving fan, sampling pumps				$0				$0
Calibration devices				$0				$0
Consultants				$0				
Telephone and Fax				$1,158				$1,216
Photocopying				$811				$852
Total Supplies & Services								
Other (detail)								
Tuition and Fees								
3 GSR In-State Fee Remissions				$28,718				$29,580
Total Other								
Subcontracts				$0				$0
Total Subcontracts								
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)								
Total Direct Costs				$243,687				$255,676
Indirect Costs				$111,784				$117,570
Total Costs				$355,471				$373,246

Project **Center for Assessment of Microbial Risk Agents**
PI **Dr. Paul Keim**
Institution **Northern Arizona University**
Indirect Cost Rates **46.8% (Year 1) 46.8% (Years 2-5)**
Project Dates 5/16/05 to 5/15/10

		Year 1 - Keim				Year 2 - Keim				Year 3 - Keim			
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
Keim, Paul		5.0%	$10,400	$2,111	$12,511	5.0%	$10,712	$2,174	$12,886	5.0%	$11,033	$2,240	$13,273
Wagner, David		5.0%	$3,300	$1,185	$4,485	5.0%	$3,399	$1,220	$4,619	5.0%	$3,501	$1,257	$4,758
Post-doctoral Researchers													
Vogler, Amy		5.0%	$2,218	$1,007	$3,225	5.0%	$2,284	$1,037	$3,321	5.0%	$2,353	$1,068	$3,421
Research Assitants													
Allender, Chris		50.0%	$8,000	$1,328	$9,328	50.0%	$8,240	$1,368	$9,608	50.0%	$8,487	$1,409	$9,896
Undergraduate		100.0%	$20,400	$1,632	$22,032	100.0%	$21,012	$1,681	$22,693	100.0%	$21,642	$1,731	$23,374
Total Personnel			**$44,317**	**$7,263**	**$51,580**		**$45,647**	**$7,481**	**$53,127**		**$47,016**	**$7,705**	**$54,721**
Travel & Meetings													
Domestic- Scientific meetings					$3,000				$3,000				$3,000
Foreign													
Total Travel					**$3,000**				**$3,000**				**$3,000**
Equipment (detail)													
Total Equipment													
Supplies & Services (by category)													
(Provide major categories, add lines as needed)													
Taq DNA polymerase					$5,250				$5,250				$5,250
Radionucleotides					$5,250				$5,250				$5,250
Dispos glass/ plasticware					$4,298				$4,298				$4,298
Misc. Biochemicals					$4,186				$4,186				$4,186
Electrophoresis reagents					$5,135				$5,135				$5,135
General project supplies, printing, telephone													
Telecommunications													
Total Supplies & Services					**$24,119**				**$24,119**				**$24,119**
Other (detail)													
Publication costs					$2,000				$2,000				$2,000
Total Other					**$2,000**				**$2,000**				**$2,000**
Subcontracts													
Total Subcontracts													
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)													
Total Direct Costs					$80,699				$82,246				$83,840
Indirect Costs					$20,740				$21,363				$22,004
Total Costs					$101,439				$103,609				$105,844

Project **Center for Assessment of Microbial Risk Agents**
PI **Dr. Paul Keim**
Institution **Northern Arizona University**
Indirect Cost Rates **46.8% (Year 1) 46.8% (Years 2-5)**
Project Dates 5/16/05 to 5/15/10

	Year 4 - Keim				**Year 5 - Keim**				**Yr 1-5**
Personnel: include each person or position on a separate line (add lines as needed)	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	**Cumulative Total**
Keim, Paul	5.0%	$11,364	$2,307	$13,671	5.0%	$11,705	$2,376	$14,081	
Wagner, David	5.0%	$3,606	$1,295	$4,901	5.0%	$3,714	$1,333	$5,048	
Post-doctoral Researchers									
Vogler, Amy	5.0%	$2,423	$1,100	$3,524	5.0%	$2,496	$1,133	$3,629	
Research Assitants									
Allender, Chris	50.0%	$8,742	$1,451	$10,193	50.0%	$9,004	$1,495	$10,499	
Undergraduate	100.0%	$22,292	$1,783	$24,075	100.0%	$22,960	$1,837	$24,797	
Total Personnel		**$48,427**	**$7,936**	**$56,363**		**$49,879**	**$8,174**	**$58,054**	$273,845
Travel & Meetings									
Domestic- Scientific meetings				$3,000				$3,000	
Foreign									
Total Travel				**$3,000**				**$3,000**	$15,000
Equipment (detail)									
Total Equipment									
Supplies & Services (by category)									
(Provide major categories, add lines as needed)									
Taq DNA polymerase				$5,250				$5,250	
Radionucleotides				$5,250				$5,250	
Dispos glass/ plasticware				$4,298				$4,298	
Misc. Biochemicals				$4,186				$4,186	
Electrophoresis reagents				$5,135				$5,135	
General project supplies, printing, telephone									
Telecommunications									
Total Supplies & Services				**$24,119**				**$24,119**	$120,595
Other (detail)									
Publication costs				$2,000				$10,000	
Total Other				**$2,000**				**$2,000**	$10,000
Subcontracts									
Total Subcontracts									
AMOUNT OF SUBCONTRACT TO BE CHARGED IC (1st 25K)									
Total Direct Costs				$85,482				$87,173	$419,440
Indirect Costs				$22,664				$23,344	$110,114
Total Costs				$108,145				$110,516	$529,554

Project	**Center for Advancing Microbial Risk Assessment**
PI	**Mitchell Small**
Institution	**Carnegie Mellon University**
Indirect Cost Rates 45% MTDC	**Fringe Benefits 26.18%**
Project Dates	5/16/05 to 5/15/10

	Year 1 - PI Name				Year 2 - PI Name				Year 3 - PI Name			
Personnel: include each person or position on a separate line (add lines as needed)	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
SMALL, MITCHELL	2.0%	**$ 2,617**	$ 685	$3,302	2.0%	**$ 2,707**	$ 709	$3,416	2.0%	**$ 2,804**	$ 733	$3,537
CASMAN, ELIZABETH A	20.0%	$ 14,730	$ 3,857	$18,587	20.0%	$ 15,243	$ 3,991	$19,234	20.0%	$ 15,777	$ 4,128	$19,905
BRUINE DE BRUINE, WENDY	10.0%	$ 4,485	$ 1,174	$5,659	10.0%	$ 4,641	$ 1,215	$5,856				
DOWNS,JULIE	20.0%	$ 15,219	$ 3,985	$19,204	19.0%	$ 14,967	$ 3,918	$18,885				
HOLBROOK, MANDI	25.0%	$ 7,926	$ 2,076	$10,002	31.0%	$ 10,173	$ 2,664	$12,837				
Graduate Assistants												
Level III, 1/2 time, six months only												
Level I, 1/2 time												
Total Personnel				**$56,755**				**$60,228**				**$23,443**
Travel & Meetings												
Domestic				$ 2,251				$ 2,328				$ 4,390
Foreign				$0				$0				$0
Total Travel				**$2,251**				**$2,328**				**$4,390**
Equipment (detail)												
Total Equipment												
Supplies & Services (by category)												
HUMAN SUBJECT PAYMENTS				$ 500				$ 500				
TECHNICAL SUPPLIES & SERVICES				$ 2,500				$ 2,575				
ADVERTISING PROCUREMENT				$ 3,050				$ 3,050				
General project supplies, printing, telephone				$ 950				$ 979				$ 212
Telecommunications												
Total Supplies & Services				$ 7,000				$ 7,104				$ 212
Other (detail)												
Tuition and Fees												
Total Other												
Total Direct Costs				$66,006				$69,660				$28,045
Indirect Costs				$ 29,703				$ 31,349				$ 12,620
Total Costs				$95,709				$101,009				$40,665

Project **Center for Advancing Microbial Risk Assessment**
PI **Mitchell Small**
Institution **Carnegie Mellon University**
Indirect Cost Rates 45% MTDC
Project Dates

	Year 4 - PI Name				Year 5 - PI Name				Yrs 1-5
Personnel: include each person or position on a separate line (add lines as needed)	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	Project Total
SMALL, MITCHELL	2.0%	**$ 2,903**	$ 760	$3,663	2.0%	**$ 3,002**	$ 787	$3,789	$17,707
CASMAN, ELIZABETH A	5.0%	$ 4,083	$ 1,070	$5,153	5.0%	$ 4,224	$ 1,106	$5,330	$68,209
BRUINE DE BRUINE, WENDY									
DOWNS,JULIE									
HOLBROOK, MANDI									
Graduate Assistants									
Level III, 1/2 time, six months only									
Level I, 1/2 time									
Total Personnel				**$8,816**				**$9,119**	$158,360
Travel & Meetings									
Domestic				$ 2,487			$2,569	$2,569	$14,026
Foreign				$0					
Total Travel				**$2,487**				**$2,569**	$14,026
Equipment (detail)									
Total Equipment									
Supplies & Services (by category)									
HUMAN SUBJECT PAYMENTS									
TECHNICAL SUPPLIES & SERVICES									
ADVERTISING PROCUREMENT									
General project supplies, printing, telephone				$ 219				$225	$2,585
Telecommunications									
Total Supplies & Services				$ 219				$225	$14,760
Other (detail)									
Tuition and Fees									
Total Other									
Total Direct Costs				$11,522				$11,913	$187,145
Indirect Costs				$ 5,183				$5,359	$84,214
Total Costs				$16,705				$17,272	$271,359

Project Center for Advancing Microbial Risk Assessment
PI James S. Koopman, M.D.
Institution University of Michigan
Indirect Cost Rates 53.0% (Year 1) 53.0% (Years 2-5)
Project Dates 5/16/05 to 5/15/10

		Year 1 - PI Name				Year 2 - PI Name				Year 3 - PI Name			
Personnel: include each person or position on a separate line (add lines as needed)		% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
Koopman, James		20.0%	$15,703	$4,868	$20,571	20.0%	$16,174	$5,014	$21,188	20.0%	$16,659	$5,164	$21,824
Koopman, James		20.0%	$5,234	$1,623	$6,857	20.0%	$5,391	$1,671	$7,062	20.0%	$5,553	$1,721	$7,274
Graduate Assistants													
TBN		50.0%	$21,505	$6,667	$28,172	50.0%	$22,150	$6,867	$29,017	50.0%	$22,815	$7,073	$29,887
Total Personnel			**$42,442**	**$13,157**	**$55,599**		**$43,715**	**$13,552**	**$57,267**		**$45,027**	**$13,958**	**$58,985**
Supplies & Services (by category)													
Six Computers @ $3000 each					$18,000								
Total Supplies & Services					**$18,000**								
Other (detail)													
Tuition @ $6891/Term * 2 Terms/Yr					$13,782				$14,609				$15,485
Biomedware					$14,530				$40,100				$41,050
Computer Connectivity					$900				$927				$955
Total Other					**$29,212**				**$55,636**				**$57,490**
Total Direct Costs					$102,811				$112,903				$116,475
Indirect Costs					$47,185				$52,096				$53,525
Total Costs					$149,997				$164,999				$170,000

Project	**Center for Advancing Microbial Risk Assessment**
PI	**James S. Koopman, M.D.**
Institution	**University of Michigan**
Indirect Cost Rates	**53.0% (Year 1) 53.0% (Years 2-5)**
Project Dates	5/16/05 to 5/15/10

	Year 4 - PI Name				Year 5 - PI Name			
Personnel: include each person or position on a separate line (add lines as needed)	% Effort	Budgeted Salary	Budgeted Fringes	Total	% Effort	Budgeted Salary	Budgeted Fringes	Total
Koopman, James	20.0%	$17,159	$5,319	$22,478	20.0%	$17,674	$5,479	$23,153
Koopman, James	20.0%	$5,719	$1,773	$7,492	20.0%	$5,891	$1,826	$7,717
Graduate Assistants								
TBN	50.0%	$23,499	$7,285	$30,784	50.0%	$24,204	$7,503	$31,707
Total Personnel		**$46,378**	**$14,377**	**$60,755**		**$47,769**	**$14,808**	**$62,577**
Supplies & Services (by category)								
Six Computers @ $3000 each								
Total Supplies & Services								
Other (detail)								
Tuition @ $6891/Term * 2 Terms/Yr				$16,415				$17,399
Biomedware				$41,900				$45,950
Computer Connectivity				$983				$1,013
Total Other				**$59,298**				**$64,362**
Total Direct Costs				$120,053				$126,940
Indirect Costs				$54,928				$58,056
Total Costs				$174,981				$184,996

Michigan State University Budget Justification

Personnel: Dr. Rose, Dr. Hashsham, Dr. Bolin, and Dr. Todd will devote 15%, 10%, 5% and 5% of their time, respectively during the academic year to this project. Summer funding for Dr. Hashsham is requested for the duration of the project. Dr. Rose will serve as the co-director (along with Dr. Haas from Drexel University). She will be responsible for oversight of the center financially, the activities of the executive steering and integration team (ESI) and will serve in the role of the QA/QC center officer. She will directly oversee methods and exposure data associated with Project I. Dr. Todd will be involved in Project V, overseeing the education program. Dr. Bolin will contribute as a co-PI to Project II, overseeing all animal studies. Dr. Hashsham will be a part of Project I assessing and methods and molecular surrogates. All other investigators' time will be contributed as a cost-sharing by Michigan State University.

One full-time staff member will be hired to complete administrative tasks for CAMRA and to assist with paperwork, data bases, web sites, educational programs and other communication programs. In addition, this individual will assist in coordination of the project's and ESI team integration effort.. . The annual salary for the staff member is $40,750 in year 1 and increases 3% in each following year.

Two post-doctoral associates will be hired 100% full time to assist in the coordination of the laboratory project and the computational risk assessment efforts. One will address the development of the BAC surrogates and methods assessment and will work directly under the supervision of Dr. Hashsham. The other will be involved in the computational efforts associated with quantitative microbial risk assessment and set up an MRA laboratory as well as assist with the educational program. This individual will work directly with Dr. Todd and Dr. Rose.

Funding for two graduate assistants is requested for the duration of the project. Salary for the graduate assistants begin at $25,000 per year and increase 3% in following years. Salaries were chosen to attract exceptional students associated in engineering, microbiology and veterinary sciences. In addition, Michigan State University will provide funding for two additional graduate students to work on CAMRA projects. Two of the graduate students will be recruited to work with Dr. Rose and Dr. Bolin on Projects I and II . All four students will be a part of CAMRA consortium of graduate students.

Fringe Benefits: Fringe benefits for faculty, student and postdoctoral salaries are charged at the University-designated rates and are listed on the budget pages.

Supplies: Supplies will be purchased and associated with administration (integration, coordination and communication), Project I, Project II and Project V. Administrative costs will support CAMRA data management, computers, software, web site, costs associated with organizing ESI team meetings. The educational costs will include the set up and development of on-line course, workshop materials and the MRA laboratory which is computer and computationally-based. The laboratory-based costs will be associated with the surrogate and methods experiments and will include costs of nucleotides, supplies for microfabrication of beads with attached molecular sequences, and supplies needed for detection of surrogates by various methods including PCR. The estimated cost of chemicals includes the synthesize and validation of oligos with fluorescent labels. PCR materials include primers, enzymes, buffers, microfuges, microfuge tubes, pipets, master mixes and gel materials. Photography materials for records of the results. The costs associated with the BAC surrogates and methods assessment

will also include supplies to grow and purify viruses. This will include cell culture flasks, culture media, and serum. For environmental samples agar, broth media, glassware, filters, petri plates will be purchased. Immunomagnetic antibodies will be purchased. General laboratory and microscopic supplies will be purchased including pipets, slides, filters and bulbs. Funds will also be used to ship samples from UA, NAU, UCB to and from MSU. Project V education supplies include laptop computers and software to conduct Monte Carlo analysis such as @Risk, Analytica and Crystal Ball. Costs for these are $1000 per laptop and $600 for educational software.

Project II associated with animal studies requires a larger investment in laboratory supplies. Dr. Bolin will require approximately a best estimate of $250,000 over the 5-year project for these experiments. In year 1, $10,000 is requested to obtain special filter top cages, aerosol delivery devices, and 50 mice to test the aerosol delivery system and to test other inoculation routes. In year 2, $40,000 is requested for mice ($7,000), animal containment space and animal care ($7500), safety supplies for animal care staff and lab personnel ($2500), student hourly help (500 hours @ $9/hr= $4500), Laboratory supplies (including: culture media, plastic ware, disposal of biohazardous waste, drugs/euthanasia materials, etc = $10,000), histopathology on tissues from mice ($7000), and Occupational Health assessments and care required to work with highly pathogenic organisms ($1500). In year 3, $40,000 is requested for mice ($7,000), animal containment space and animal care ($7500), safety supplies for animal care staff and lab personnel ($2500), student hourly help (500 hours @ $9/hr= $4500), Laboratory supplies (incl: culture media, plastic ware, disposal of biohazardous waste, drugs/euthanasia materials, etc = $10,000), histopathology on tissues from mice ($7000), and Occupational Health assessments and care required to work with highly pathogenic organisms ($1500). In year 4, $40,000 is requested for mice ($7,000), animal containment space and animal care ($7500), safety supplies for animal care staff and lab personnel ($2500), student hourly help (500 hours @ $9/hr= $4500), Laboratory supplies (incl: culture media, plastic ware, disposal of biohazardous waste, drugs/euthanasia materials, etc = $10,000), histopathology on tissues from mice ($7000), and Occupational Health assessments and care required to work with highly pathogenic organisms ($1500). In year 5, $10,000 is requested for mice ($2,000), animal containment space and animal care ($1500), safety supplies for animal care staff and lab personnel ($500), student hourly help (100 hours @ $9/hr= $900), Laboratory supplies (incl: culture media, plastic ware, disposal of biohazardous waste, drugs/euthanasia materials, etc = $2,600), histopathology on tissues from mice ($1000), and Occupational Health assessments and care required to work with highly pathogenic organisms ($1500).

Travel: A total of $60,000 in travel funds are requested for each year of the project. The total amount was based on an estimated 30 trips per year at $2000 per trip. These funds will be used to bring the ESI team and project teams together, as well as support the Center Advisory Board. Funds are to allow the investigators, post-doctoral associates and students working on CAMRA projects to meet with collaborators at participating universities, attend scientific meetings to present research findings, and to attend EPA and DHS meetings.

Subcontracts: The total costs for each year are given for the subcontracts. Detailed budgets are provided for each university.

Indirect Costs: The indirect cost rate is 51% for all five years of the project.

DREXEL UNIVERSITY BUDGET JUSTIFICATION

Personnel: Professor Haas will serve as co-director of CAMRA and as PI for the dose-response project. His salary for Year I is computed at $165,000 (9 month basis). The level of effort budgeted for Professor Haas is 12% for the Administrative Core in both the summer and academic year for all five years of the project. For the Dose-response project his effort is budgeted at 17% of the summer in the first three years and 12% of the summer in the last two years. We are also incorporating a 67% appointment of a project coordinator (salary $40,000) who will provide support for financial management, maintenance of all Drexel records on CAMRA, and coordination on operational matters with MSU and other institutions.

Patrick Gurian will serve as PI for the Assessment-Analysis Interface project. His salary for Year I is computed at $85,000 (9 month basis). A constant 8% effort is budgeted for summer support through the first four years of the project with 11% effort in Year V. Academic year support is budgeted at 18% for Year I, 9% for Year II, 8% for Year III, 3% for Year IV, and 0% for Year V. This schedule will allow for a concentrated initial effort with a goal of rapidly developing results that can be used to guide CAMRA's subsequent research efforts.

Rosina Weber will serve as PI for the Knowledge Management, Transfer, and Learning team at Drexel. Her salary for Year I is computed at $75,000 (9 month basis). Her academic year effort is budgeted at 22%, 22%, 0%, 25%, and 22% in Years I-V, respectively. Her summer effort is budgeted at 8%, 47%, 9%, 5%, and 19%, in Years I-V, respectively. Co-investigator Michael Atwood will be supported at 27% during the summer of Year I, and co-investigator Hyoil Han will be supported at 9% of academic year time in Years III and IV.

Graduate research assistants are budgeted on a 12-month basis for a 20 hour per week effort. In addition, graduate assistants receive tuition benefits. Tuition charges based on 30 credits (quarter system basis) are included – which is considered a full time load for graduate research assistants at Drexel University.

Student support for the Dose-Response project is budgeted at 1.5 students in Year I, 2.5 students in Years II and III, and 1.5 students in Years IV and V. Drexel University will contribute as a cost share 40% of the tuition charges for the 2.5 students in Year II, 26% of the 2.5 students in Year III, and 23% of the 1.5 students in Year IV. For Year V, funding for an undergraduate in the amount of $12,000 is requested. This individual will assist with contract closeout, mechanics of publication, etc. This will provide for roughly 20 hours/week of effort as the current (04-05 year) hourly figures for undergraduate employees range from $9 - $15/hour.

Salary and tuition support for one graduate student for the Assessment-Analysis Interface project is budgeted for Years I-V.

Support for one doctoral student is also budgeted for the Knowledge Management, Transfer, and Learning project for the five years, starting at $19,500 in Year I. Tuition charges for this student will be contributed by Drexel University as a cost share. Professional programmers will also be hired to assist with this project at market rates which are currently around $50/hour. $22,693 is budgeted in Year I (roughly a day a week) and $10,178 in Year II (half a day a week) to hire a

professional PHP programmer to support the initial effort of setting up the database. In Year III $20,186 is budgeted (close to a day a week) to hire a professional Oracle programmer to support the preparation of the data warehouse.

The salary figures in all cases (for faculty and students) incorporate a 5% annual escalator.

Fringe Benefits :The standard fringe benefit rate is 23.8% on non-student salaries.

Travel: Travel funds are for each year of the project. These will be used for travel to professional meetings, such as the annual meeting of the Society for Risk Analysis, to present results of the research. The funds for investigators to travel to the STAR meetings and to visit collaborators at consortium institutions are also included. For example, Dr. Rosina Weber (PI for the Knowledge Management, Transfer, and Learning Project) will visit all consortium institutions in Years I and II in order to educate collaborators about the knowledge repository. This includes travel by the CAMRA co-director to coordinate the activities of the different institutions.

Equipment: No equipment expenses are budgeted for the Drexel portion of the project.

Supplies: The supplies budget will include three computers dedicated to this project, one for the Knowledge Management, Transfer, and Learning Project (to be purchased in Year I to host the knowledge repository) and two for the dose-response Project (to be purchased in Years I and IV). In Year III, the Knowledge Management, Transfer, and Learning Project will purchase an Oracle license for building the data warehouse. The remainder of the budget will include data storage devices, computer software, and upgrades.

Other: The item for other consists of graduate research assistant tuition and publication expenses.

Indirect Charges: The Drexel indirect cost rate is 50% of MTDC, which includes fringe benefits, <u>but excludes</u> tuition.

University of Arizona Budget Justification

Personnel: One postdoctoral fellow at 75% time (full time annual salary $35,000) in agricultural and biological systems engineering (ABE) is request to aid with the dispersion and transport modeling. This individual will also be responsible for data collection and analyses. A 25% graduate assistant (full time salary $42,248) in ABE is also requested to aid in the conduct of experiments. A 50% time graduate assistant (full time annual salary of ($36,000) is requested for construction and evaluation of the surrogates. They will also be involved in the conduct of laboratory and field experiments. A 3% increase in salary adjustment per year is requested. Dr. Gerba (Co-principal investigator), and Choi (Co-PI) will provide 10% of their time without charge to the project. Dr. Pepper (Co-Investigator) will provide 5% of his time without charge to the project. A graduate student (50%) will be provided by the Water Quality Center as matching. This student will work on integration of the exposure data generated a this part of the center with other emphasis areas of the center i.e. modeling of exposure and infectivity data, transport data and exposure in different environments. In addition, they will be involved in assessment of pathogen persistence and detection in aquatic environments.

Fringe Benefits: Salaries and fringe benefits are set by the University of Arizona. The University of Arizona requires that tuition remission be required as part of the fringe benefits for graduate research assistantships.

Travel: Travel to from the University of Arizona Campus and the Environmental Research Laboratory (site of the Water Village) (15 miles round trip) $1035 (200 trips@ $0.345/mile). Two trips to Northern Arizona University for two persons (1400 miles = $483; meals = $359; Room = $400) $1242. Travel to two professional meeting for the principal investigators. Travel for Dr. Gerba to the Annual Meeting of the American Society for Microbiology (airfare $400; meals $200; room $500) $1100. Dr. Choi to the Water Quality Technology Conference $1123.

Equipment: No equipment of a value of more than $5,000 is requested.

Supplies: Laboratory supplies are required for the growth and detection of surrogate microorganisms to be used in this study. This includes enzymes and other reagents for the detection of microorganisms by the polymerase chain reaction, purification kits for preparation of environmental samples, bacteriological media, centrifuge tubes, supplies for construction of viral like particles (reagents, enzymes, cloning supplies), bottles for sample collection, disposable pipettes and test tubes, petri dishes, [purchase of bacteria, virus, cloning vectors ($1,000), biohazard bags, disposable gloves, beakers, flasks, acoustic flow meters to measure transient fluid flow ($2,000), control units, solenoid values, data accusation units, DHI-MOUSE software for water transport simulations ($3,000), laptop commuter for data acquisition at he Water Village; mass flow meters ($3,000), hardware and sensor replacement and maintenance at he Water Village, software for drinking water network flow simulations ($3,000). Office Supplies: photocopying, postage, phone, etc. ($1,000 per year). In year 3 and 4 $2,000 is requested for page charges for publication (current costs range from $50 to $125 per page) and $3,000 in year 5.

UNIVERSITY OF CALIFORNIA, BERKELEY BUDGET JUSTIFICATION

Personnel: Dr. Mark Nicas, Principal Investigator, will devote 25% time to the project in each of Years 1 through 5. His projected annual salary for Year 1 is $100,878. $25,219 is requested for year 1. The benefits rate for Dr. Nicas is 17% resulting in a cost of $4,287. A 5% increase in salary for Dr. Nicas is projected for each of Years 2 through 5.

Dr. Joe Eisenberg, Co-Investigator, will devote 25% time to the project in each of Years 1 through 5. His projected annual salary for Year 1 is $79,968. $19,992 is requested for year 1. The benefits rate for Dr. Eisenberg is 17% resulting in a cost of $3,399. A 5% increase in salary for Dr. Eisenberg is projected for each of Years 2 through 5.

Dr. Alan Hubbard, Statistician, will devote 10% time to the project in each of Years 1 through 5. His projected annual salary for Year 1 is $67,728. $6,773 is requested in year 1. The benefits rate for Dr. Hubbard is 17%, resulting in a cost of $1,151. A 5% increase in salary for Dr. Hubbard is projected for each of Years 2 through 5.

Dr. Tom McKone, Risk Analyst, will devote one month time to the project in each of Years 1 through 5. His projected annual salary for Year 1 is $144,630. $12,053 is requested for year 1. The benefits rate for Dr. McKone is 17%, resulting in a cost of $2,049. A 5% increase in salary for Dr. McKone is projected for each of Years 2 through 5.

Dr. William Nazaroff, Engineer, will devote one month of time in the summer to the project in each of Years 1 through 5. The projected one month summary salary for Year 1 is $12,556. The benefits rate on this salary is 12.7%, so the requested benefits amount is $1,595. A 5% increase in salary for Dr. Nazaroff is projected for each of Years 2 through 5.

Arthur Reingold, MD, Epidemiologist, will devote one-half month of time in the summer to the project in each of Years 1 through 5. The projected one-half month summary salary for Year 1 is $7,559. The benefits rate on this salary is 12.7%, so the requested benefits amount is $960. A 5% increase in salary for Dr. Reingold is projected for each of

Judy Tam, Project Assistant, will prepare financial reports, prepare invoices, and handle the distribution of funds to the UC Berkeley project personnel. She will devote 7% time to the project in each of Years 1 through 5. Her projected annual salary for Year 1 is $44,946, the requested salary amount is $3,146. The benefits rate for Ms. Tam is 22%, so the requested benefits amount is $692. A 5% increase in salary for Ms. Tam is projected for each of Years 2 through 5.

Three Graduate Student Researchers, Step II, (names to be announced) will work on the project in each of Years 1 through 5. In each year, each GSR will work 9 months at 49.9% time, and 3 months at 100% time. The projected GSR II annual full-time salary rate in Year 1 is $32,154 with a 2% benefits rate during the academic year and a 4% benefit rate during the summer. Per GSR, for 9 months the requested salary amount is $12,034, and for 3 months the requested salary amount is $8,038, for a total of $$20,072 in Year 1. The benefits rate on the academic year salary is 2% and the rate on the summer salary is 4%, so the requested benefits amount is

$563 in Year 1. A 5% increase in salary for each GSR is projected for each of Years 2 through 5. In addition, we request in-state fee remission for each GSR. For Year 1, the projected fee per GSR for the academic year is $8,203. $24,609 is requested. For Year 2, there is a projected 10% increase of in-state fees; therefore, for Year 2 we request $27,069. For Year 3, there is a projected 3% increase of in-state fees; therefore, for Year 3 we request $27,882 for fee remission. For Year 4, there is a projected 3% increase of in-state fees to; therefore, for Year 4 we request $28,719. For Year 5, there is a projected 3% increase of in-state fees; therefore, for Year 5 we request $29,580.

Project Supplies and Expenses: In Year 1, $2,000 is requested for office supplies; $1,000 is requested for computer expendables; $2,500 is requested for materials and construction of a particle test chamber; $4,293 is requested for air moving fans and sampling pumps; $2,000 is requested for calibration devices for the particle experiments; and $5,000 is requested for laboratory reagents, sampling media, glassware, pipettes, tubing and other laboratory-related supplies. In Year 2, $2,000 is requested for office supplies; $1,000 is requested for computer expendables; $3,021 is requested for a computer; $1,000 is requested for two laser jet printers; and $10,000 is requested for laboratory reagents, sampling media, glassware, pipettes, tubing and other laboratory-related supplies. In Year 3, $2,200 is requested for office supplies; $1,000 is requested for computer expendables; $5,031 is requested for two computers; and $10,000 is requested for laboratory reagents, sampling media, glassware, pipettes, tubing and other laboratory supplies. In Year 4, $2,200 is requested for office supplies; $1,000 is requested for computer expendables; $4,520 is requested for two computers; and $12,000 is requested for polystyrene spheres, laboratory reagents, sampling media, glassware, pipettes, tubing and other laboratory supplies. In Year 5, $2,400 is requested for office; $1,000 is requested for computer expendables; $2,690 is requested for a computer; and $15,000 is requested for polystyrene spheres, laboratory reagents, sampling media, glassware, pipettes, tubing and other laboratory supplies.

Photocopying: In Year 1, $700 is requested for photocopying charges for progress reports to principal investigators at Michigan State University and research data to present at scientific conferences. We request a 5% increase in each of Years 2 through 5. That is, in Year 2 we request $1.05 \times \$700 = \$735$, in Year 3 we request $1.05 \times \$735 = 772$, and so forth.

Travel: In each of Years 1 through 5, one trip to a scientific conference is requested for both Dr. Nicas and Dr. Eisenberg to present research results. In each of Years 1 and 2, the projected cost is $2,000 per conference trip. In each of Years 3 and 4, the projected cost is $2,100 per conference trip. In Year 5, the projected cost is $2,200 per conference trip.

NORTHERN ARIZONA UNIVERSITY BUDGET JUSTIFICATION

Personnel: With the exception of an undergraduate student who will be recruited specifically for this study, all of the individuals who will be involved with this project are currently working in the Keim Genetics Laboratory (KGL) at NAU. Thus, budgeted salaries are based on their actual, existing salaries. Fringe benefits are calculated for each individual according to NAU Human Resources Departmental guidelines, available at http://www.nau.edu/sps/FBRATES.HTM. The indirect costs are only associated with direct salary costs at a rate that is NAU's federal standard (46.8%).

Paul Keim, Ph.D. (Principal Investigator; 5%) – Dr. Paul Keim, the principal investigator, is the Cowden Endowed Chair in Microbiology at Northern Arizona University (NAU). He has a joint appointment at the Translational Genomics Research Institute (TGen), where he is the Director of Pathogen Genomics. He has lead efforts to identify strains in several bioterrorism events, including the 2001 anthrax letter attacks. In recognition of the importance of microbial forensics, the Arizona Board of Regents established the Dangerous Pathogen Center at NAU under Dr Keim's direction. His efforts have lead to more than 130 scientific publications in the area of genetics and genomic analysis. In 2002, he organized an American Academy of Microbiology colloquium to guide the novel science of microbial forensics (Keim, 2003). Dr. Keim has Q-clearance (TS) and is an affiliate researcher with Los Alamos National Lab. In addition, he serves on the FBI Scientific Working Group for Microbial Forensics. Dr. Keim will be responsible for directing the overall research project, both scientifically and managerially.

David M. Wagner, Ph.D. (Co-Investigator; 5%) – Dr. David Wagner, co-principal investigator, is a Research Associate and Senior Lab Coordinator in the KGL. Dr. Wagner specializes in phylogenetic, spatial, and temporal analyses that are crucial for assay development and modeling of disease occurrence. His recent paper in plague population analysis (Girard and Wagner et al., 2004) contains a paradigm for high resolution subtyping and modeling for understanding the significance of DNA matches or near matches. Dr. Wagner will also serve as a project coordinator, overseeing the flow of laboratory information into the modeling phase.

Amy J. Vogler, Ph.D. (Post-Doctoral Researcher; 5%) – Dr. Amy Vogler, post-doctoral researcher, specializes in the molecular sub-typing of biological threat agents, including *B. anthracis*. Dr. Vogler has extensive experience handling BSL-2 level pathogens and has undergone a Department of Justice Background Investigation that authorizes her to work with select agents. She will oversee or personally conduct many of the laboratory analyses described in the proposal, curate and analyze data generated in the project, and assist with manuscript preparation.

Christopher J. Allender, B.S. (Research Assistant; 50%) – Mr. Allender is a graduate research assistant in Dr. Keim's laboratory where he focuses on developing and validating real-time PCR assays for species and strain-specific identification of bacterial pathogens. Mr. Allender's recent work in this area has resulted in the development of a TaqMan RT-PCR assay that detects SNPs that are diagnostic for major groups within *Yersinia pestis*, the causative agent of plague. He is trained in BSL-2 level practices and has a Department of Justice Security Risk Assessment clearance that permits him to work with select agents. His responsibilities on the research team

will include assay design, testing, and validation, as well as collection and processing of environmental samples. It is anticipated that Mr. Allender will complete his M.S. (2007) degree while working on this project, under the supervision of Drs. Keim and Wagner.

Undergraduate Student (100%) – We will recruit an undergraduate research assistant to work on this project. This individual will focus on performing the molecular subtyping protocols described in this proposal, as well as collecting and processing environmental samples for DNA based analyses.

Equipment: None.

Supplies: To perform the proposed analyses, we will require funding in each year to cover expenses associated with purchasing reagents and expendable supplies. We are requesting $27,000 in each year to cover these expenses, with the following breakdown in costs: *Taq* DNA polymerase - $5,875, primers and probes - $5,875, disposable glass/plasticware - $4,855, miscellaneous biochemicals - $4,725, and electrophoresis reagents - $5,670.

Travel: We request $3,000 to support travel to 2-3 national scientific meetings each year.

Other Expenses: We request $2,000 to cover publication expenses in each year.

CARNEGIE MELLON UNIVERSITY BUDGET JUSTIFICATION

Salaries and Wages: Dr. Casman will devote 20% of her time in years 1-3 and 5% in years 4-5 (calendar year basis) to this project. Dr. Small will devote 2% (academic year) for all 5 years. Dr. Bruine de Bruin is committed for 10% (calendar year) of her time in years 1 and 2, and Dr. Downs, 20% and 19% for those years. Ms Holbrook will devote 25% and 31% of her time (calendar year) to this project in years 1 and 2.

A professional transcriptionist will be hired part time in years 1 and 2 to transcribe 50 1-hour interviews.

Fringe Benefits: Fringe benefits for faculty, student and postdoctoral salaries are charged at the University-designated rates and are listed on the budget pages.

Total Salaries and Fringes: are listed on the budget pages.

Nonexpendable Equipment: None required

Supplies: Recruiting the subjects will be handled by a professional service which will provide the number subjects of specified backgrounds at the required times. The interviews will be by phone and will also be scheduled by this service. (Our previous experience has shown that this is less expensive and time consuming than doing the same in-house.)

Funds are included to cover the costs of preparing and publishing the results of research conducted under the award, including costs of reports, reprints, page charges or other journal costs including necessary illustrations or photographic reproductions.

Travel: Funds are to allow the investigators to attend 1 meeting a year at other CAMRA Universities and for one person to go to one scientific conference in year 3 to present the findings.

Indirect Costs: The indirect cost rate(s) are charged at the appropriate rate that has been negotiated by the awarding organization with the cognizant Federal negotiating agency. The "Negotiated Rate Agreement" is for Carnegie Mellon University.

Total Costs: The total costs requested for the five year period are $271,360.

University of Michigan Budget Justification

Personnel: Support for Dr. Koopman is requested for each year of the project for a total of $145,616 . Two lines are used in the budget table to determine his salary because he has a 9-month academic appointment and 3-month summer appointment, both of which are used to calculate annual salary. Dr. Koopman will dedicate 20% of his effort to this project. A 50% graduate assistant (full time salary starting at $21,505) is also requested. The graduate student is essential for completing model construction and analysis. A 3% increase in salary adjustment per year is requested.

Fringe Benefits: Salaries and fringe benefits are set by the University of Michigan. The fringe benefit rate for both faculty and graduate students is 31%.

Travel: No travel funds are requested.

Equipment: No equipment of a value of more than $5,000 is requested.

Supplies: Six computers, costing $3000 each for a total of $18,000, are required for the project. Dr. Koopman will be responsible for computer models using data generated by other collaborators. As a result, adequate computer capabilities are required to create and process the models. The computers will be purchased in year 1 and used for the duration of the project.

Other: Tuition for the graduate student assistant is requested for the five years of the project. The rates are based on tuition costs for two terms per year, beginning at $6891 per term and increasing 6% each following year. Biomedware is a local software firm that has developed the software that will be used for computer modeling. The models link deterministic and stochastic models. The software cannot be used directly for our purposes, however, it will have to be considerably modified. The computer connectivity fee is the fee the School of Public Health charges for computers to connect to university servers.

Indirect costs: The current rate for indirect costs set by the University of Michigan is 53%.

QUALITY ASSURRANCE STATEMENT

The goal of the QA/QC program is to have established protocols for development of the experimental data, documentation, data analysis, management, and reporting to insure high-quality performance. Joan Rose, co-director of CAMRA, will be responsible for the QA/QC program for the Center. As the QA/QC officer, she will be responsible for monitoring the various project and ensuring collaborators are following established QA/QC protocols. CAMRA will maintain records on each project which will contain:

- Names of personnel working on each project
- Nature of project
- Test systems
- Dates project started and completed
- Status of project
- QA/QC protocols for each project
- Compliance reports

Because a large part of the Center's mission deals with data management, comprehensive up-to-date records are essential. CAMRA will maintain records detailing the management of the Center as well as laboratory protocols. These records will include:

1. Quality Policy Statement and Commitments by Top Management
2. Organization and Management Structure
3. Relationship between Management, Support Services, and Quality System
4. Job Descriptions of Key Staff
5. Identification of Key Signatories for the Laboratory
6. Laboratory Equipment and Calibration and/or Verification Test Procedures Used
    6.1 Laboratory Equipment
    6.2 Calibration of Laboratory Equipment
    6.3 Procedures for Achieving Traceability of Measurements
7. Laboratory Setup and Procedures
8. Procedure for Handling Collected and Submitted Samples
9. Corrective Action Contingencies
10. Procedures for Data Reduction, Verification, Validation, and Reporting
11. Procedures for Establishing that Personnel are Adequately Trained
    11.1 Training and certification of personnel
    11.2 Training on new equipments and procedures
12. Procedures for Protecting Confidentiality and Proprietary Rights
13. Record Keeping and Reporting of Results

The officer, or approved administrative staff member, will review reports and conduct inspections of facilities to ensure compliance with QA/QC protocols. Inspection reports will include date and time of inspection, the test inspected, any problems encountered, and any action to be taken to remedy the problems. Quarterly progress reports will be sent to the co-directors of CAMRA and the major co-investigators. The progress reports will summarize the status of each project, if any problems have been identified and actions taken to come into compliance with

QA/QC plans. All QA/QC procedures will be available to EPA and DHS. EPA and DHS can also request the officer for written certification that QA/QC protocols are being implemented.

All of the principal investigators will be responsible for ensuring compliance with established QA/QC plans in their laboratories. The study design and methodology for each project is descibed in each project description. All QA/QC plans will comply with ANSI/ASQC E4, *Specifications and Guidelines for Quality Systems for Environmental Data Collection and Environmental Technology Programs.* Each project leader will also periodically submit reports to the QA/QC officer. Reports will include the date and time, name of individual, status of project, and compliance with the project's QA/QC plan. The ESI and scientific advisory committee will provide input on experimental methodology and design for each project prior to data collection to ensure the success of meeting research goals.

APPENDIX: SUPPORT LETTERS