Center for Advancing Microbial Risk Assessment
Annual Report

Submitted to

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National Center for Environmental Research
U.S. Environmental Protection Agency
1025 F. Street, NW, Room 3500
Washington, D.C. 20004

And

Mr. Matthew Clarke
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Washington DC

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Overall Accomplishment

The Center for Advancing Microbial Risk Assessment (CAMRA) was established on September 1, 2005. The following are highlights of administrative accomplishments

- September 2005 CAMRA was established, began arranging subawards, contracts, and working on a Quality Management Plan.
- February 2006 Organized and held an All Principal Investigators (PIs) Organizational meeting.
- April 2006 All subawards and contracts were finalized for Drexel University, University of Arizona, Northern Arizona University, University of Michigan, Carnegie Mellon University, University of California, Berkeley
- June 2006 Quality Management Plan was completed and approved.
- August 2006 Quantitative Microbial Risk Assessment (QMRA) Summer Institute was held at Michigan State University

Official work for all contracts and requirements were completed between April to June 2006. Overall accomplishments for projects to date are summarized in the attached table 1 and summarized below. PI specific reports are available.

The objectives of CAMRA's Projects I - V have not changed as stated in the original proposal. The Knowledge Management (KM) system is being used by CAMRA to capture key literature, projects in progress and completed work. Thirty eight learning units (LUs) were created to achieve the aims toward the ultimate goal of a data and knowledge warehouse. These LUs are entered by each PI, usually with attachments with the paper, protocols or data, they are approved by Dr. Rosina Weber and reviewed by the Directors. Ten LUs have been completed to date, 27 are currently in progress, and there are ~10 more LUs which are waiting approval. Other important outputs include 1 proceedings paper published, 2 peer reviewed publications (in press), and 3 presentations.

CAMRA ran its first workshop, "QMRA Summer Institute", at Michigan State University, East Lansing, MI from August 4th to 13th, 2006. Important outputs associated with the Summer Institute include lecture materials and instructional computer based programs for learning QMRA and four case studies; groundwater contamination, norovirus outbreak, pathogen survivals on fomites, and exposure to pathogens in sewage-contaminated beach sand.

There has been no change of PIs. In addition to the 19 PIs, 4 postdoctoral fellows, 15 graduate students, and 1 administrative assistant contributed to the CAMRA's Year-1 accomplishments. It is pleasure to report that two of CAMRA's graduate students, Sheng Li and Ian Spicknall, won the First Place Award for Doctoral Program Day Poster Session, University of Michigan in March 2006. The title of the poster was "Risk Assessment for Biosecurity".

The few scientific difficulties encountered during the early center activities were regarding the extensive literature reviews. There were numerous articles on topics where

no quantifiable information was included in the published literature. The CAMRA investigators quantified the results from different studies and normalized the data. These normalized data are currently available for CAMRA through the Knowledge Management (KM) system.

All data obtained were assured based on the CAMRA Quality Management Plan, via the KM assurance . The Quality Management Plan is currently under revision. One key set back was the loss of the Quality Assurance Officer, QAO, Dr. Jamie Willard. Dr. Rose and Dr. Haas are currently working with each University to replace the QAO to minimize the impacts on the grant and the PIs objectives. In this case the QAPP from each PI will be transferred to the new QAO and the audits and site visits will then be organized.

The membership of the Science Advisory Committee is being finalized. We have had several scientists decline because of limited available time. It is anticipated that most SAC members will be at the Feb. all PI meeting.

Future activities will include a symposium and a presentation at the meeting for the Society for Risk Analysis and one presentation at the Society for Practical Aspects in Knowledge Management) in December 2006, An all PI meeting is being planned for Feb. 28-March 1 at Carnegie Mellon University. A one-day QMRA workshop for American Society for Microbiology is planned for May 2007 and has been accepted. Synopsis of key outputs and outcomes from the Project I ~ V are given below.

Project I: Exposure, Detection, Fate and Transportation of Agents

Charles P. Gerba[1], Chris Choi[1], Ian Pepper[1], Syed Hashsham[2], Paul Keim[3], Mark Nicas[4], and William Nazaroff[4]; [1]University of Arizona, [2]Michigan State University, [3]Northern Arizona University, [4]University of California, Berkley

The primary accomplishments in Project I include 1) assessment of detection methods for *Bacillus anthracis*, 2) investigation of potential Anthrax surrogates, 3) assessment of decay constants for Biological Agents of Concern (BAC) and virus surrogates on fomites, 4) examination of the EPANET water quality model, and 5) updating a Discrete-Time Markov Chain model for airborne BAC.

The most sensitive detection method for Anthrax was identified to be real time polymerase chain reaction (PCR). Knowledge of detection limits of the various available methods is key to the quantification of risk and the ability to interpret what a non-detect really means (Figure 1). *Bacillus thuringiensis*, which was found to be the best Anthrax surrogate, and will be practical for studying the fate and transport of Anthrax on fomites and in air and water. Virus survival (inactivation rates) were summarized. T-90s were in days to months on fomites for enteric viruses, compared to hours to days for respiratory viruses (Figure 2). These data will be used in predictive models for assessing transport and fate. Experiments at the Water Village showed that initial computational fluid dynamics simulations consistently underestimated mixing. The improvement of the existing code will be important for addressing potential intentional or accidental contamination events. The Markov chain particle model developed for virus-particle

transmission and was initially evaluated against the appropriate published data. The model predictions reasonably agreed with the experimental observations. The model will facilitate predicting airborne concentrations and deposition of BAC in indoor environments following intentional or accidental releases.

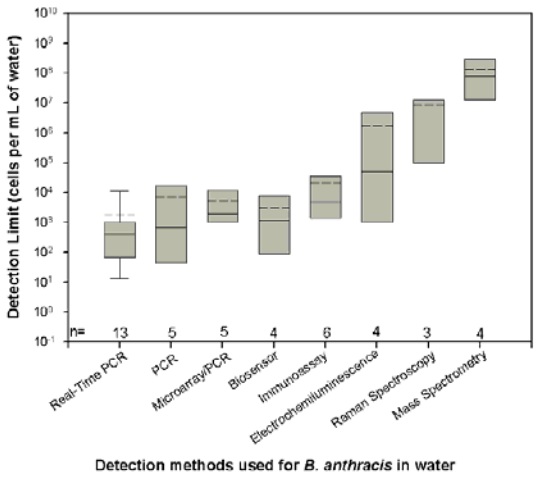

Figure 1: Detection limit for various methods available to detect *B. anthracis* in water.

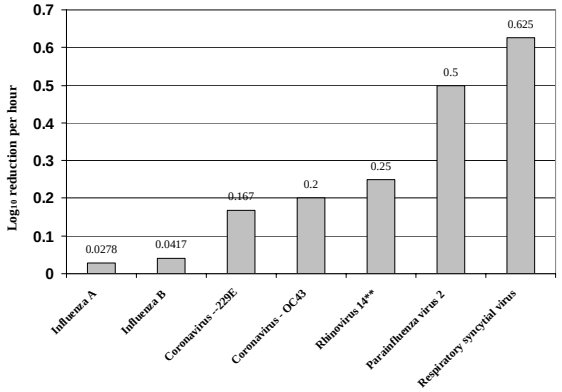

Figure 2: Respiratory virus inactivation rates (K_i).

Project I will continue to pursue identification of parameters that affect fate and transport of BAC, and development of new experimental protocol for the assessment of fate and transportation of BAC in aerosols and water distribution systems using BAC surrogates.

Project II: Infectious Disease Models for Assessing Microbial Risk and Developing Control Strategies

Joseph N.S. Eisenberg and James Koopman, University of Michigan

The primary accomplishments in Project II include 1) creation of a database that structures pathogens by characteristics, 2) development of models for contamination on single objects, 3) transmission in single venues, and 4) transmission in multiple venues.

The structure of the database contains information relevant to transmission, e.g. infection and immunity, survivability, transfer coefficients, and dose-response. This database structure will ultimately become a means for an alternative taxonomic classification of infectious pathogens.

Project II will continue to address the database and summarize data needs, and analyze the data. The Year-2 intervention study will complete a single object model with advice on sampling strategies, develop a single venue intervention scenario using single venue model, develop multiple venue intervention scenarios using the multiple venue model, and complete the influenza model at the college campus level, and then use it to help redesign an intervention study.

Project III: Dose Response Assessment
Charles N. Haas, Drexel University

The primary accomplishments in the Project III include 1) determination of dose response model fitting for inhalation of *Bacillus anthracis* spores in different host species and 2) fitting dose response models to *Yersinia pestis* (Y. pestis) dosing data for; wild caught squirrels and lab reared rock squirrels via subcutaneous inoculation.

A key outcome from the *B. anthracis* work is the finding that the dose-response in monkeys and in guinea pigs from inhalation is identical. This lends substantial support to the hypothesis that the same dose response relationship can be used to project the human risk of exposure from inhalation of *B. anthracis* spores. The R source codes can be used for various different microorganisms for which different dose response models can be compared and fitted to data that may be found. The source code written has been verified with prior research (Haas, C.N., 2002), using data from Haas (2002) on inhalation exposure to *Bacillus anthracis* spores supporting the presented model as the best fit (exponential model) with the same parameters, and on ingestion exposure of human rotavirus.

Project III will develop dose-response information for exposure to Variola (smallpox), dose-response information for exposure to hemorrhagic viruses (e.g., Lassa, Marburg, Ebola) and novel dose-response models incorporating time to infection and physiological parameters and review of outbreak studies for validation data sets

Project IV: Assessment-Analysis Interface
Patrick Gurian[1], Elizabeth Casman[2], Mitchell Small[2], and Julie Downs[2], [1]Drexel University, [2]Carnegie Mellon University

The primary accomplishments Project IV include development of a scenario for a plague release, identification of critical decisions and choices, identification of opportunities/needs for risk communications, and demonstration of a novel risk communication planning method.

The major advancement is a new method for risk communications planning for complex scenarios. The point of the analysis was to try to anticipate the information needs people would have if there were a big urban aerosol plague attack. The current planning ignores animals, but animals play a part in human plague ecology. This study identified population sectors with specialized information needs and the kinds of information that would probably be wanted. It also developed a method for risk communication planning that probes complicated scenarios for the unexpected consequences/dependencies in order to avoid being blind-sided if there were an actual attack.

One finding from this analysis is that response planning should consider the possibility of the bioattack agent being multiply drug resistant. The mental models work in Year 2 will examine aspects of this issue, particularly vaccination acceptance.

The decision to certify a site as clean is being explored in order to better define the key uncertainties in this decision. This effort has developed quantitative values for surface

concentrations corresponding to a 1 in 1 million fatality risk for past anthrax exposure. These values are intended only as example calculations, not as regulatory guidance. Thus the ultimate outcomes are guidance for regulators as they seek to develop response plans and priorities for research to reduce key uncertainties.

Project IV will compare the Bayesian hierarchical dose-response modeling for anthrax with the classical dose-response models fit by Project III, expand the existing compartment modeling of anthrax into a system of coupled indoor-outdoor models with a re-suspension component, including simplified removal factors for HVAC filters and coils.

Project V: Knowledge Management, Transfer, and Learning
Rosina Weber, Michael Atwood, and Hyoi Han, Drexel University

The primary accomplishments in the Project V include design of the knowledge repository, implementation and test of the knowledge repository, investigation of the domain structure for QMRA, and presentation of CAMRA KR version 1.0 to members (referred to in the report as the KM, Knowledge Management system).

The system has been in operation since July 20, 2006 in its version 1.0. The concept of an evolving learning unit refers to adapting the repository main artifact to the needs and culture of this community. Some aspects of the evolution are already completed and implemented, such as the inclusion of a field for Outcomes. The most important distinction from the original plan is the incorporation of reporting capabilities. Such capabilities require the incorporation of other items such as outputs, currently under study. The main expected outcome is achieved on a prototypical level, "Communication tool to address critical data gaps in the MRA Framework and provide information to MRA professionals to reduce uncertainties in MRAs." Project V has a unique integration to all other projects because it is responsible for their integration. The connection with all other projects is through the collaboration, sharing, and integration among them (Figure 3).

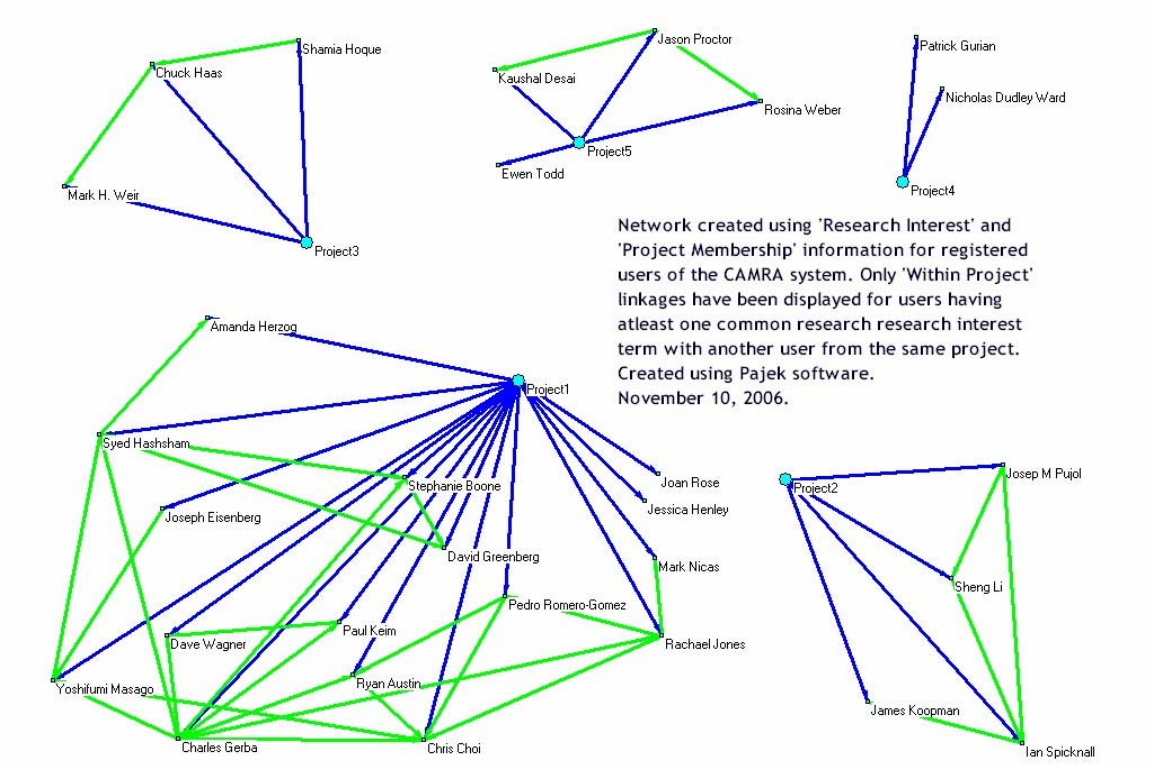

Figure 3: Network created using “Research Interests” and “Project Membership” information for users registers on the CAMRA system.

The Year-2 tasks for the Project V will include revising learning units, building version 2.0 of knowledge repository, defining domain structure for QMRA, and applying reasoning methods on the knowledge repository.

Integration of Projects I, II, III and IV.

Integration of the dose-response**environmental exposure**population models is moving forward via Project II working directly with Projects I and III. In addition an anthrax integration model is being developed to connect detection sensitivity and specificity with dose response (Project I, III and IV) to be presented at Gordon Research Conference on " Chemical & Biological Terrorism Defense" in January, 2007.

Appendices

Table 1: Accomplishments and Ongoing Research Activities during the Year-1

Investigators	Status of Year-1 Tasks	Publications/Presentations/ Workshops
Dr. Joan B. Rose Co-Directors Michigan State University (Postdoctoral fellows) Dr. Yoshifumi Masago Dr. Tomoyuki Shibata (Administrative Assistant) Allena R. Tapia	(Completed) ▪ Hosted the Quantitative Microbial Risk Assessment (QMRA) Summer Institute (In progress) ▪ Gathering data on Cryptosporidium outbreak at Seneca Park, NY in Aug 2005: LU 608 ▪ Investigation of sampling methods for virus on fomites; PRD1 recovery and inactivation coefficient; LU 609 ▪ Investigating the risk of pathogen exposures to children from sewage-contaminated beach sand risk assessment, pathogens, sewage spill, beach sand: LU 619 ▪ Proposing the QMRA summer institute 2007: LU 459	(Workshop) ▪ QMRA Summer Institute, MI ▪ Infectious Disease Informatics, IL ▪ National Academy of Science**,** From Exposure to Human Disease: Research Strategies to Address Current Challenges ▪ National Conference on Environmental Sampling and Detection for Bio-Threat Agents, NY
Dr. Charles P. Gerba Dr. Ian L. Pepper University of Arizona Project I (Postdoctoral fellow) Dr. Stephanie Boone (MS student) Jessica Henley	(Completed) ▪ Inactivation rates for influenza A & B, rhinovirus 14, cornavirus (oC43 and 229e) Parainfluenza 2, respiratory synctial: LU 540 (In progress) ▪ Developing fate and transport models for BAC and other microbes (respiratory viruses), die off rate or inactivity rate on fomites: LU 439 ▪ Developing fate transport models for BAC and other microbes enteric virus decay or inactivation rates on fomites: LU 583	(Publication) ▪ The significance of fomites in the spread of respiratory and gastrointestinal disease, *Applied and Environmental Microbiology*, In Press. (Workshop) ▪ QMRA Summer Institute, MI
Chris Choi, Ph.D. University of Arizona Project I (MS Student) Ryan Austin (Ph.D. Student) Pedro Romero-Gomez	(Completed) ▪ Experimental dispersion of chemicals in pressurized water systems: LU 538 ▪ Examination of the Perfect Mixing Assumption in Water Quality Models Dispersion patterns in water distribution systems: LU 706 (In progress) ▪ Modeling and Experimental Verification of Water Distribution Systems: LU 456 ▪ Revised EPANET water quality model: LU 560 ▪ Describing experimental setup for analyzing chemical dispersion in junctions of water distribution systems: LU 561 ▪ Complex Network Modeling Prediction using Water Quality Models and Artificial Neural Network: LU 701 ▪ Pattern Recognition and Axial Dispersion Artificial Neural Network: 707	(Presentation & Proceeding) ▪ Transport Phenomena at Intersections of Pressurized Pipe Systems, 2006, 8th Annual Water Distribution Systems Analysis Symposium**,** Cincinnati, OH. (Workshop) ▪ QMRA Summer Institute, MI

Investigators	Status of Year-1 Tasks	Publications/Presentations/ Workshops
Dr. Syed Hashsham Michigan State Univ. Project I (MS Student) Amanda Herzog	(Completed) ▪ Detection limit *B. anthracis* in water: LU 631 (In progress) ▪ Detection limit of all methods for *B. anthracis:* LU 425 ▪ Detection limit *B. anthracis* in air: LU 740 ▪ Detection limit *B. anthracis* in soil: LU 742 Evaluating quantum dots (QDs) as surrogates: Activity is release, dispersion, and recovery of surrogates; Matrix is air, water, soil, or surfaces: LU 738	(Workshop) ▪ MRA Summer Institute, MI
Dr. Paul Keim Dr. Dave Wager Northern Arizona Univ. Project I (Ph.D. Student) David Greenberg	(In progress) ▪ Investigating potential surrogates for *B. anthracis*: LU 552 ▪ Developing reliable and reproducible spore purification method *B thuringiensis, B. anthracis*: LU 675	(Workshop) ▪ QMRA Summer Institute, MI
Dr. Mark Nicas Dr. William W. Nazaroff UC Berkley Project I (Ph.D. Student) ▪ Rachael Jones	(In progress) ▪ Particle fate and transport modeling airborne release of particles: LU 362 ▪ Designing aerosol release experiments for model validation: LU 362	(Workshop) ▪ QMRA Summer Institute, MI
Dr. Joseph Eisenberg Dr. James Koopman University of Michigan Project II (Postdoctoral fellow) Josep M. Pujol (Ph.D. Students) Ian Spicknall Sheng Li	(In progress) ▪ Modeling Contamination of Individuals and the Environment Using an Individual Based Model Assuming Random Mixing in a Single Venue: LU 497	(Presentation) ▪ Risk Assessment for Biosecurity", Doctoral Program Day Poster Session, University of Michigan ▪ Assessing Infection Risks and Control Options when Transmission is Person-to-Person via Multiple Routes across Diverse Venues, Society for Risk Analysis (accepted) (Workshop) ▪ QMRA Summer Institute, MI

Investigators	Status of Year-1 Tasks	Publications/Presentations/ Workshops
Dr. Charles N. Haas Co-Directors, Drexel University Project III (Ph.D. Students) Mark H. Weir Sushil Tamrakar (MS Student) Bishel Kurungattu	(Completed) ▪ Dose Response Modeling Fitting for Inhalation of Bacillus Anthracis Spores in a Different Host Species: LU 240 (In progress) ▪ Modeling of airborne aerosols with charge transport, indoor air, computational fluid dynamics: LU 405 ▪ Fitting Dose Response Models to *Yersinia pestis (Y. pestis)* Dosing Data for, Wild Caught Squirrels and Lab Reared Rock Squirrels via Subcutaneous Inoculation: LU 715 ▪ Fitting Dose Response Models for Data of Bacillus Anthracis Inhalation Exposure of; Rhesus Monkeys, Guinea Pigs and Rabbits: LU 716	(Presentation) ▪ DHS Centers for Excellence Meeting , DC (Workshop) ▪ QMRA Summer Institute, MI
Dr. Patrick Gurian Drexel University Project IV (MS Students) Nicholas Dudley Ward Ashley Kenyon	(In progress) ▪ Bayesian Hierarchical Dose Response Modeling for Anthrax: LU 498	(Presentation) ▪ Responding to anthrax contamination: Listening to surfaces and talking to people, Society for Risk Analysis (accepted) (Workshop) ▪ QMRA Summer Institute, MI
Dr. Elizabeth Casman Dr. Mitchell Small Dr. Julie Downs Carnegie Mellon University Project IV	(Completed) ▪ Review of studies documenting behaviors or expressed willingness to comply with recommendations influencing personal risks during epidemics and bioterrorism events: LU 572 ▪ Expert model development for mental models interviews. (Plague scenario) (In progress) ▪ Methodology for risk-communication content-planning for complex bioterrorism scenarios ▪ Expert model development for mental models interviews. (Anthrax scenario)	(Workshop) ▪ QMRA Summer Institute, MI (Publication) ▪ No time to think: Preparing for Post-bioattack Communications" (in review) (Presentation) ▪ Public Communication Needs for Plague Bioterrorism Incidents" Soc. Risk Anal. Ann. Mtg., Dec 2006

Investigators	Status of Year-1 Tasks	Publications/Presentations/ Workshops
Dr. Rosina Weber Dr. Michael Atwood Dr. Hyoi Han (Ph.D. Students) ▪ Jason M. Proctor ▪ Marcia Morelli	(Completed) ▪ Designing CAMRA KR version 1.0: LU 621 and 743 ▪ implementing and testing the knowledge repository version 1.0: LU 730 and 745 ▪ Presenting CAMRA KR to members version 1.0: LU 734 and 749 (In progress) ▪ Bibliometric domain analysis on KM: LU 238 ▪ Investigating learning units in version 1.0: LU 732 and 746 ▪ Investigating QMRA domain structure: LU 733 and 748 ▪ Monitoring and maintaining the knowledge repository: LU 735, 750	(Publication and presentation) ▪ Identifying the Core of an Emerging Multidisciplinary Domain. In: Grove, A. (ed.), Proceedings of the 69th Annual Meeting of the American Society for Information Science and Technology, vol. 43. (Publicationand presentation) ▪ Designing a Knowledge Management Approach for the CAMRA Community of Science. U. Reimer and D. Karagiannis (Eds.): PAKM 2006, LNAI 4333, pp. 315–325. Springer-Verlag Berlin Heidelberg. (Workshop) ▪ QMRA Summer Institute, MI