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
Department of Homeland Security
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.

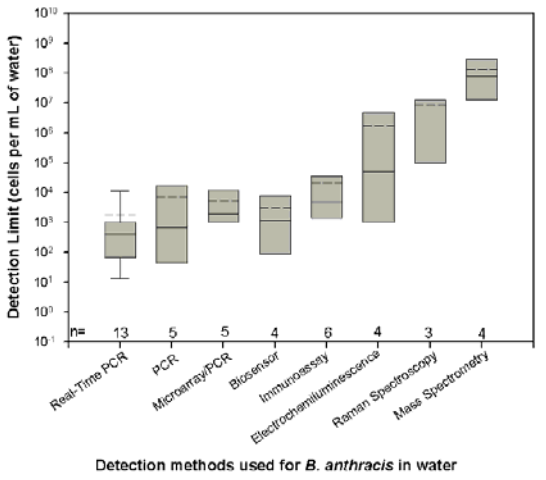

Figure 1: Detection limit for various methods available to detect *B. anthracis* in water.

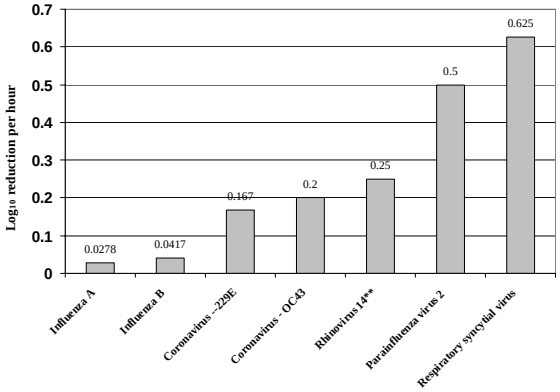

Figure 2: Respiratory virus inactivation rates (K_i).

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).

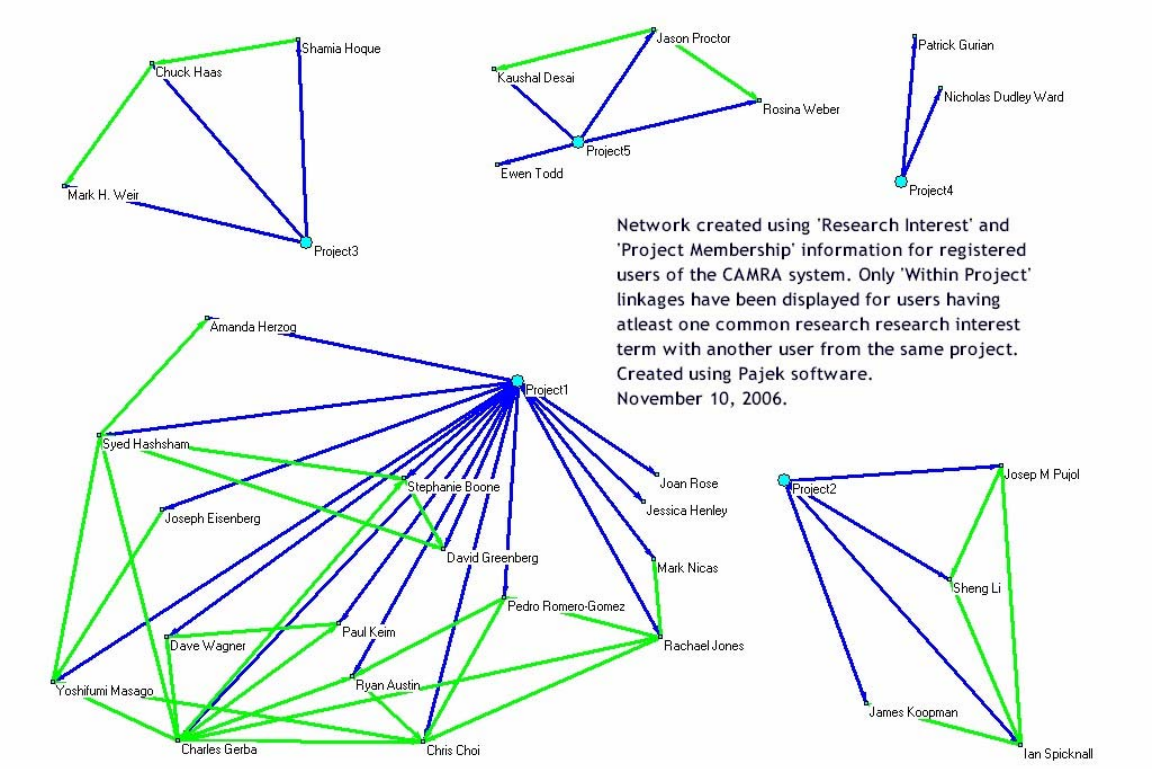

Figure 3: Network created using “Research Interests” and “Project Membership” information for users registers on the CAMRA system.

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

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

Investigator: Charles P. Gerba and Ian L. Pepper

Project Goals (from proposal, additional goals):

Tasks for Year (I):

The primary task goals of year one were to conduct an extensive literature review to identify data gaps on the survival of agents of concern on fomites and potential surrogates, the development of criteria for selection of surrogates, and develop a protocol for assessing decay constants for agents of concern and surrogates on fomites.

Research Activities:

Literature reviews were conducted on the decay of agents of concern. From this review normalized decay constants were developed. This information was prepared for publication so that it can be available for the use in exposure models. This review also identified environmental factors of greatest importance in predicting the decay of agents of concern and where data gaps exist. This information was then used to define experimental conditions for assessing the decay of potential surrogates for agents of concern were data is lacking.

A set of criteria was developed for the selection of surrogates and is currently being prepared for input by the other investigators in CAMRA.

Initial laboratory experiments have been conducted on methods for the detection of surrogates on fomites for use in assessment of decay rates and for detection in indoor environments.

Background and prior research:

While the study of microbial persistence on fomites has been conducted by numerous investigators no attempt to normalize the data from different studies has been. In addition, identification of all the significant factors influencing the decay has not been summarized until this study. While various surrogates have been used for agents of concern, the selection of criteria has not yet been defined, especially in reference to objectives.

Research Contributions this Year:

LU 544

To be useful in model predictive models on the fate of agents of concern information on their decay on fomites needs to be normalized from various studies published in the literature. The existing literature on the survival of enteric and respiratory viruses was reviewed and data on virus decay was normalized against environmental conditions reported by the various students review. This data is now available for use in models to

predict survival of these agents on fomites. It was found that enteric viruses survive for days to months on surfaces compared to hours to days for respiratory viruses.

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Outputs:

8.1 Students Supported and/or Graduated:

Stephanie Boone (postdoctoral fellow – research associate)
Jessica Henley (M.S. student, in progress)

8.2 Publications:

Boone, S. A. and C. P. Gerba 2006. The significance of fomites in the spread of respiratory and gastrointestinal disease. Applied and Environmental Microbiology, In Press.

8.3 Patents

None

8.4 Presentations:

None

8.5 Participation or organization of workshops:

CAMRA Summer Institute

8.6 Case studies, algorithms developed: **None**

8.7 Human Resource Development: **None**

8.8 Other (consulting, interviews, etc.): **None**

8.9 Funds Leveraged (additional funding, resources for free):

Outcomes:

The publication of normalized decay rates for viruses on fomites allows for the prediction of the survival agents of concern on common indoor objects (fomites). This can be used in models to assess the risk of infection to first responders or other exposed individuals after the release of an agent of concern in buildings.

Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

My student and I are working together with Dr. Choi and his students on development of viral and other tracer tests for the distribution system network.

We have met with Dr. Syed Hashsham this year several times to discuss the development of detection methods for surrogate organism and the types of surrogates that might be most useful for release into various environments. We have been working with Dr. Paul Keim and his graduate student about the parameters for developing data on the persistence and detection of *Bacillus antrhuis* and selected of appropriate surrogates for this pathogen. We will be working with Dr. Keim's group to develop comparative data on decay models of agents of concern and surrogates in various environments.

I also met twice this year with Dr. Mark Nicas to discuss the development of data on the decay of agents of concern on fomites and in aerosols. We are working together to develop the testing protocol we will use to assess model development on the fate of aerosolized surrogate in buildings.

I have met several times with Dr. Joan Rose to work on the methods and conditions to be used for the detection and assessment of decay rates on fomites for agents of concern and surrogates.

Tasks for Next Year:

Assess the use of coliphages MS2 or PRD1 as tracer in distribution system research using the experimental systems at the Water Village (in collaboration with Dr. Choi), starting with the pipe intersection problem.

Complete laboratory research of data base on the decay rates of surrogates and agents of concern on fomites under a variety of conditions for use in predictive models. This will be done in conjunction with Dr. Keim's group.

Development normalized decay rates for surrogates and agents of concern in surface and drinking water for use in fate and transport models. This will be done both through a review of the literature and laboratory experimentation.

Project: Exposure: Detection, Fate and Transport of Agents

Investigator: Christopher Y. Choi

Project Goals (from proposal, additional goals): Modeling BAC in water systems (model development and design; field studies utilizing the Water Village)

Tasks for Year (I):

The primary task is to establish a research infrastructure at the newly-established Water Village at the University of Arizona and to carry out modeling and experiments. The system is designed based on EPANET. Computational Fluid Dynamics (CFD) is used to examine the accuracy of the EPANET Water Quality model, which is revised if necessary. An Artificial Neural Network (ANN) model is tested to identify the unknown parameters that lead to concentration histories, release locations, and the release time of hypothesized biological agents.

Research Activities:

Water quality models at intersections of pressurized pipe systems have been investigated. The movement of chemicals or biological agents is examined via computational fluid dynamics simulations. A series of computational simulations using selected geometries are carried out at various Reynolds numbers. Boundary conditions, turbulence intensities, convergence criteria, and mesh sizes are thoroughly evaluated. The present parametric study focuses particularly on pipe intersections to characterize complex mixing phenomena in pressurized water distribution pipe networks. Experimental verifications have been carried out at the Water Village.

A 5 x 5 water distribution network was designed and divided into six regions. Each region was assumed to have a random water demand. An injection point for chemicals was set at the reservoir. EPANET was used to perform steady-state simulations given the demands, and the average chemical concentration for each region was estimated. Therefore, a set of six water demands and their corresponding averaged concentrations made up one scenario. Several scenarios were created in order to generate training and testing data required for a back-propagation Artificial Neural Network (ANN) with six input (water demands) and six output (average concentration) units. A high correlation between the predicted (with ANN) and simulated (with EPANET) concentrations has been observed. This correlation decreased for regions near the reservoir. Concentrations in the regions away from the reservoir were consistently predicted more accurately.

Background and prior research:

Fowler and Jones (1991) first raised a question about the accuracy of the perfect mixing assumption at pipe junctions. More than a decade later, van Bloemen Waanders et al. (2005) noted the significance of the issue in water quality modeling. Using experimental data (with NaCl) and two-dimensional computational fluid dynamics (CFD) simulation tools, they found that the simplified assumption of complete mixing at pipe junctions in current water quality models indeed caused significant inaccuracies.

Essential References

Fowler, A. G. and P. Jones, (1991), "Simulation of Water Quality in Water Distribution Systems". AwwaRF and US EPA Conference of Water Quality Modeling in Distribution Systems, Cincinnati, Ohio.

van Bloemen Waanders, B., G. Hammond, J. Shadid, S. Collis and R. Murry (2005). A comparison of Navier Stokes and network models to predict chemical transport in municipal water distribution system. *ASCE Congress*, Anchorage.

Research Contributions this Year:

LU 456 and LU 706.

Computational results are compared with experimental results to examine water quality models at intersections of in water distribution systems. The water quality model integrated with an existing computer program (EPANET) was evaluated based on the computational and experimental data. Initial computational fluid dynamics simulations consistently underestimated mixing, and experimental data are utilized to reexamine turbulent mixing by adjusting the turbulent Schmidt number. Corrections based on computational results are incorporated into the existing code as an example case study. The improvement of the existing code may be important not only to predict concentrations of chemical species such as chlorine in water distribution systems, but also to prepare for potential intentional and accidental contamination events. Computational results must be further calibrated and verified through lab- and field-scale experiments.

LU 701 and LU 707.

First, a 5 x 5 water distribution network was designed. The system was divided into six regions. Each region was assumed to have a random water demand. An intrusion location was designated within the network as a reservoir. EPANET was used to perform steady-state simulations, and an average concentration for each region was estimated. Thus, a set of six water demands and their corresponding average concentrations were considered as a scenario. Several scenarios were utilized in order to generate training and testing data required for a back-propagation Artificial Neural Network with six input (water demands) and six output (average concentration) units. A high correlation between the predicted (with ANN) and simulated (with EPANET) concentrations was observed. However, this correlation decreased for regions near the reservoir. Concentrations in regions further from the reservoir were consistently predicted more accurately. The network is currently under construction at the Water Village.

A 10 x 10-node network was examined using the EPANET, which included four intrusion points and four monitoring (sampling or sensor) locations. A series of steady-state simulations were carried out to define various scenarios that were generated for training and testing of the ANN. Each scenario included: a) random water demands set at each node, b) an intrusion point activated, and c) the four "readings" from monitoring

locations (concentration at those nodes as calculated by EPANET water quality model). The determination of the intrusion point based on the ANN was not yet highly correlated to actual injection point, unlike the 5 x 5 cases. This may be due to the architecture and characteristics of the chosen ANN. Probabilistic functions must be included in the hidden layer in order to account for the stochastic nature of this problem.

Outputs:

8.1 Students Supported and/or Graduated:

Ryan Austin (M.S. Student, in progress)
Pedro Romero-Gomez (Ph.D. Student, in progress)

8.2 Publications:

Conference Proceedings: Romero-Gomez, P., C. Y. Choi, B. van Bloemen Waanders, and S. McKenna, Transport Phenomena at Intersections of Pressurized Pipe Systems, 2006, 8th Annual Water Distribution Systems Analysis Symposium, Cincinnati, OH.

8.3 Patents: **None**

8.4 Presentations:

Romero-Gomez, P., C. Y. Choi, B. van Bloemen Waanders, and S. McKenna, Transport Phenomena at Intersections of Pressurized Pipe Systems, 2006, 8th Annual Water Distribution Systems Analysis Symposium, Cincinnati, OH.

8.5 Participation or organization of workshops:

CAMRA Summer Institute

8.6 Case studies, algorithms developed: **None**

8.7 Human Resource Development: **None**

8.8 Other (consulting, interviews, etc.): **None**

8.9 Funds Leveraged (additional funding, resources for free): **The Water Distribution Network Laboratory was constructed at the Water Village with the state funding. We expect expansion of the laboratory. The laboratory will be connected to Dr. Gerba's Microbiology Laboratory.**

Outcomes:

Computational and experimental analyses are part of the efforts for (i) formulating an accurate modeling of water quality and (ii) developing prediction tools. As

utilities change from having a single mission of supplying water to consumers to also having a security mission, these tools used for network analysis will have to evolve to better simulate solute transport. The first-year work is an initial step in providing the experimental, CFD-, and ANN-based improvements to these network analysis and prediction models. Our study will impact a wide variety of network analyses including prediction of disinfectant residuals, optimal locations for water quality sensors, prediction models for early warning systems, numerical schemes for inverse source identification, and quantitative risk assessment.

Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

Computational and experimental work in collaboration with Sandia National Laboratories – two refereed journal manuscripts are in preparation.

Pattern recognition work is under consideration in collaboration with the University of Cincinnati.

Collaboration with micro-fluidic device and spectroscopy experts within the University of Arizona (Drs. Riley and Yoon)

My students and I are working together with Dr. Gerba and his student and postdoctoral fellow (Jenifer Henley and Stephanie Boone). For future collaboration efforts, I have been communicating with Drs. Syed Hashsham, Paul Keim, and Patrick Gurian.

Tasks for Next Year:

Complete turbulent mixing at intersections using experimental and computational approaches. Submit one or two refereed journal papers. Create an LU.

Set up and evaluate a modular 5 x 5 water distribution network. Establish various scenarios using EPANET. – A potential LU.

Inject MS2 or PRD1 into the experimental systems at the Water Village (in collaboration with Dr. Gerba). Start with the intersection problem. – A potential LU.

Establish prediction models using ANNs based on experimental data and EPANET simulation results for a 5 x 5 network. - A potential LU.

Explore complex models such as 10 x 10 and/or irregular water distribution networks.

Project: I

Investigators:

- Dr. Paul Keim
- Dr. Dave Wagner

Project Goals (from proposal, additional goals):

- selection of potential surrogate for Bacillus anthracis
- collection of laboratory data for selection of potential surrogates
- provide parameters for fate and transport models
- validation of detection methods

Tasks* for Year (I):

- What is the best surrogate for Bacillus anthracis both theoretically and experimentally?
- We hypothesize that Bacillus thuringiensis is most likely the best candidate, and we will conduct experiments to show the similarity between the characteristics of the spores

Research Activities (First field in learning units, starts w/ verb in -ing form, e.g., investigating):

- investigating potential surrogates for Bacillus anthracis and identifying data gaps in our knowledge and generating a review document
- developing reliable and reproducible spore purification method
- generating comparative data on the persistence (i.e. fate and transport) of BACs and surrogates on fomites

Background and prior research (from learning units of the type Things I have read, those essential references you want to include; from Year II, include summary of previous years):

a) endnote library

Research Contributions this Year (how you advanced MRA, contributions and results from completed learning units; please list the numbers of the learning units, as follows:

1.1.in progress unit 552
1.2.others are in progress, but have not been approved yet.

Outputs:

8.1 Students Supported and/or Graduated: PhD support for David Greenberg
8.2 Publications
8.3 Patents:
8.4 Presentations:
8.5 Participation or organization of workshops:
8.6 Case studies, algorithms developed:
8.7 Human Resource Development:
8.9 Other (consulting, interviews, etc.):
8.10 Funds Leveraged (additional funding, resources for free):

Outcomes (how your contributions can be used to better society):

- From an initial literature search and comparative investigation our primary target for a non pathogenic Bacillus anthracis surrogate is Bacillus thuringiensis. We will be able to use this surrogate in a wide array of environmental experiments including water distribution and aerosol experiments

Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

a) We collaborate with Dr. Chuck Gerba and Dr. Chris Choi

Integration with other projects (association between units in different projects):

a) Our work is associated with learning units 425, 439, 456, 464, 544, 578, and 583

Tasks for Next Year (see definition below):

- Comparison of several surrogate possibilities for Bacillus anthracis.
- Determine real world parameters for fate and transport models by experiments in air, soil, and on fomites.

Anticipated Technical Results and Developments (examples of potential learning units for next year, within possible also include potential outcomes):

- We plan to validate the use of Bacillus thuringiensis as a surrogate for Bacillus anthracis by direct comparison of their persistence in water, fomites, and soil.

* **Tasks** are collections of research questions, problems, or hypothesis whose developments (contributions) may be described as learning units.

1. Project: Development of a Discrete-Time Markov Chain Model for the Within-Room Transport and Fate of Airborne Microbial Agents of Concern

Note: The official start date of the subaward for UC-Berkeley was September 1,2005, but grant funds were not available at UC-Berkeley until April 20,2006.

2. Investigators: Mark Nicas, PhD, CIH (PI) and William W. Nazaroff, PhD

3. Project Goals: There are three 5-year project goals, although only the first goal was to be addressed in Year 1. The three project goals are: (i) to develop and validate a Markov chain model to predict airborne particle-associated microbial transport and fate in indoor environments; (ii) to measure the resuspension into air of particle-associated microbes due to human activity; and (iii) to determine the particle size distribution of respiratory aerosol.

4. Tasks for Year 1 (September 1,2005 through August 31,2006):

Task 1 – Refine a simple Markov chain model to include particle transport by gravitational settling and particle loss by deposition onto the floor and other room surfaces.

Task 2 – Develop a method for translating velocity vector and turbulent intensity values, as generated by computational fluid dynamics modeling or direct measurement, into transition probabilities for the Markov chain particle model.

Task 3 – Initially validate the Markov chain particle model via comparing its predictions against appropriate published data.

Task 4 – Construct a test chamber or, in the alternative, arrange for the use of a test chamber or room in which to conduct aerosol release experiments for model validation.

5. Research Activities:

Refining a simple Markov chain model (Task 1) – The Markov chain model for transport and fate of gas-phase contaminants was extended to particles. Gravitational settling was modeled by a first-order rate dependent on particle aerodynamic diameter, and deposition was modeled based on published algorithms for deposition velocity. The model accounts for particle transport via advective flow, turbulent diffusion and gravitational settling, and particle loss from room air by deposition onto the floor and other room surfaces (e.g., walls, ceiling) and by the room exhaust airflow.

Developing a method for incorporating information on air velocity and turbulent intensity values (Task 2) – The following approach was delineated. A three-dimensional air velocity vector can be posed at each room position at each moment in time. This vector can be measured with directional anenometry equipment, or by computational fluid dynamics (CFD) modeling. The distribution of three-dimensional vectors over time at the room position forms a type of "wind rose". The average of this distribution is the average velocity vector; in turn, the average vector is decomposed into average components along the orthogonal x, y and z axes. The magnitude (speed) of each average component (e.g., $\overline{\mathbf{X}}$) is used to assign a rate of particle movement due to advective flow along the corresponding axis. The difference between each instantaneous component vector and its average vector (e.g., $\mathbf{X} - \overline{\mathbf{X}}$) is defined as a residual vector **Xres**. The distribution of the magnitude (speed) of the residual, denoted $|\mathbf{Xres}|$, has mean $\mu_{|\mathbf{Xres}|}$ and variance $\sigma^2_{|\mathbf{Xres}|}$. Similar distributions of residual speeds pertain along the y and z axes. A turbulent intensity metric denoted *k* is the square root of the sum of the variances of the three residual speed distributions. If the three distributions of residual speeds are independently and identically distributed (or treated as such for simplicity), the turbulent diffusion coefficient D_T in the Markov chain model is a linear function of the turbulent intensity metric *k*. In summary, D_T is an idealized parameter that permits symmetry in the dispersion of a particle along three orthogonal axes in the Markov chain model, and under special conditions it is a function of the turbulent intensity metric used to quantify variability in air speeds along these same axes.

Initially validating the Markov chain model using published data (Task 3) – As a first step, we considered published experimental data for the floor deposition of cobalt oxide particles released in a building lobby (E Sajo, et al., "Spatial distribution of indoor aerosol deposition under accidental release conditions," *Health Physics 83*:871-883, 2002). Sajo and colleagues conducted four replicate tests of the release, and sampled deposition at approximately fifty floor positions. The cobalt oxide particle size distribution, and average air velocities at numerous room positions, were reported. The Markov chain particle model predicted a pattern of floor deposition similar to the observed pattern, with maximum floor deposition occurring near the release position. The predicted mass deposition at approximately 50% of the floor positions was within the 95% confidence interval for the average mass observed to deposit at these same locations across replicate runs of the release experiment.

Acquiring a test chamber for particle release experiments (Task 4) – Dr. Nicas and Rachael Jones (UC-Berkeley PhD student) toured the Water Village (WV) facilities at the University of Arizona in May 2006, and met with Dr. Christopher Choi and Dr. Charles Gerba. The WV has an experimentation room that is appropriate for the aerosol release experiments planned for model validation. Agreement was reached that the WV room could be used for these experiments. The latter work would involve both inert particles and particles carrying a surrogate microbial agent of concern. In addition, Dr. Choi agreed that his research group would be able to estimate the room's air velocity and turbulent intensity fields via CFD modeling. The latter modeling would permit comparing predictions concerning particle deposition and air concentrations made by the Markov chain versus CFD modeling approaches.

6. Background and prior research: A Markov chain model was developed previously to describe the transport and fate of gas-phase contaminants in indoor air. The model accommodated transport by advective airflow (bulk flow in an average direction) and turbulent diffusion (random air motion superimposed on the directional advective flow), and removal via exhaust airflow from the room. This work was presented in: Nicas M, **"**Modeling turbulent diffusion and advection of indoor air contaminants by Markov chains," American Industrial Hygiene Association Journal, Volume 62, pp 149-158 (2001). An application of the general Markov chain technique was modeling the airborne dispersion of small-diameter respirable particles carrying *M. tuberculosis* bacilli emitted by a patient with pulmonary tuberculosis, and estimating the consequent infection risk to room occupants. Because small-diameter particles have low gravitational settling rates, they were approximated as gas-phase contaminants. This work was presented in: Nicas M, "Markov modeling of contaminant concentrations in indoor air," American Industrial Hygiene Association Journal, Volume 61, pp 484-491 (2000). The current project extends the technique to supermicron particles which have substantial gravitational settling rates. The refined model includes the added transport mechanism of gravitational settling, and the added removal mechanism of deposition onto the floor and other room surfaces. In addition, the current project seeks to incorporate spatial information on air velocity and turbulent intensity to better assign the directional probabilities of particle movement.

7. Research Contributions in Year 1: The research conducted in Year 1 is described in Item 5, "Research Activities".

Task 1 is 75% completed. Remaining issues involve modeling of particle deposition onto room walls and the ceiling, and assigning initial dispersion if the released aerosol.

Task 2 is 50% completed. Remaining issues involve condensing the CFD output at thousands of room positions into transition probabilities for fewer cells in the Markov

matrix, and translating the geometry of the CFD node system to the simpler geometry of the Markov chain model.

Task 3 is 100% completed. However, if we can locate other detailed data sets on particle deposition and/or room air particle concentrations following test aerosol release, we would compare the observations against predictions made by the Markov chain model.

Task 4 is 90% completed. Although access to the University of Arizona WV experimental room has been secured, the aerosol work has yet to be scheduled.

8. Outputs:

8.1 Students Supported and/or Graduated: The grant supported Rachael Jones, a PhD student, during the Summer 2006.

8.2 Publications: None at this time. However, we have drafted a manuscript titled "A Markov Chain Model for Supermicron Particle Transport and Fate in Indoor Air." The manuscript describes our work on Tasks 1, 2 and 3 to date. The manuscript will be submitted to Journal of Occupational and Environmental Health.

8.3 Patents: None

8.4 Presentations: None

8.5 Participation or organization of workshops: Rachael Jones participated in the CAMRA Summer Institute on Quantitative Microbial Risk Assessment, in August 2006.

8.6 Case studies, algorithms developed: The work conducted for Task 1 involved refining the Markov chain model, which can be considered an algorithm. The work conducted for Task 3 was a type of case study, because we considered the experimental data published by E Sajo, et al. (2002): "Spatial distribution of indoor aerosol deposition under accidental release conditions," *Health Physics 83*:871-883.

8.7 Human Resource Development: None

8.8 Knowledge Transfer: None yet beyond the CAMRA Knowledge Repository

8.9 Other (consulting, interviews, etc.): None

8.10 Funds Leveraged (additional funding, resources for free): None

9. Outcomes:

Once more rigorously validated, the Markov chain particle model would have diverse applications. It would facilitate predicting airborne concentrations and deposition of microbial agents of concern in indoor environments following intentional or accidental releases. It would also have broader public health applications, for example, predicting airborne concentrations and deposition of nonviable but toxic particulate contaminants due to releases in occupational and residential indoor environments.

10. Collaboration with other Projects:

We are collaborating with Dr. Christopher Choi and Dr. Charles Gerba at the University of Arizona on aerosol release experiments involving both inert particles and particles carrying a surrogate microbial agent of concern. The information on aerosol deposition that comes from these experiments will be used in Dr. Choi's and Dr. Gerba's project on the transport and fate of microbial agents of concern on fomites and room surfaces. However, we are not involved in Dr. Choi's and Dr. Gerba's separate project on the transport and fate of microbial agents of concern in water distribution systems.

11. Integration with other projects:

Please see Item 10, "Collaboration with Other Projects".

12. Tasks for Year 2:

Task 1 – Complete mathematically refining the Markov chain particle model. Resolve issues related to the modeling of particle deposition onto room walls and the ceiling, and assigning initial dispersion locations of the released aerosol.

Task 2 – Delineate a procedure for condensing CFD output on room air velocity and turbulence intensity fields into transition probabilities for the Markov matrix. Translate the geometry of the CFD node system to the simpler geometry of the Markov chain model.

Task 3 – completed

Task 4 – Schedule the aerosol release experiments at the University of Arizona WV experimental room.

Task 5 – Conduct the aerosol release experiments using both inert particles and particles carrying a surrogate microbial agent of concern. Component subtasks are (i) finalizing the decision on the inert particle sizes, nature of the particles, and analytical methods; (ii) finalizing the decision on the microbial agent of concern (e.g., a bacteriophage with size parameters similar to the smallpox virus), the appropriate particle size, and the analytical method; (iii) finalizing the decision on the aerosol generation procedures; (iv) acquiring the equipment for generating the aerosols; (v) acquiring the equipment for sampling air and surfaces for the test particles; (vi) acquiring expertise in generating the aerosols; and (vii) conducting replicate trials of the aerosol release experiments. Given the approximate 8-month delay in receiving the subaward funding, it is anticipated that the aerosol release experiments will extend into Year 3 of the grant.

Task 6 – Start to analyze the experimental aerosol release data. Data on particle concentrations in air and deposition onto the floor and walls at different room positions will be compared with predictions made by the Markov chain particle given, alternatively, (i) judgmental estimates of room air velocities and turbulence versus, or (ii) CFD estimates of room air velocities and turbulence. Should grant funds permit purchasing a three-dimensional anenometer, direct measurement of air velocities at numerous room positions would be conducted. These measurements would permit examining the accuracy of CFD modeling in predicting the air velocity and turbulent intensity fields.

Task 7 – If sufficient aerosol release experiments are conducted, draft a manuscript reporting the data and the performance of the Markov chain model.

13. Anticipated Technical Results and Developments:

Please see Item 10, “Outcomes”.

Project: Validation of detection methods: (Part of Project I. Exposure: Detection, Fate and Transport of Agents)

Investigators: Syed Hashsham

Project Goals (from proposal, additional goals): Document the frequency distribution of detection limit for various methods used to detect biological agents of concern (BAC) in water, air, soil, and other matrices. Evaluate the suitability of quantum dots as a surrogate for BAC.

Tasks* for Year (I):

(i) Review of detection methods for surrogates

(ii) Evaluation of quantum dots (QDs) as surrogates

The focus of Year 1 activities was on *Bacillus anthracis.*

Research Activities (First field in learning units, starts w/ verb in -ing form, e.g., investigating):

Investigating detection limit for *Bacillus anthracis* in water, air, soil, and other matrices

Evaluating Quantum Dots (QDs) as surrogates of BAC in release, dispersion, and recovery experiments in air, water, soil, or surfaces

Background and prior research (from learning units of the type Things I have read, those essential references you want to include; from Year II, include summary of previous years):

Frequency distribution of detection limit of various methods for B. anthracis: The amount of literature published on *B. anthracis* is considerable. We were able to locate more than 1300 journal articles using a number of keywords. These references are available in an EndNote file upon request. This list was analyzed by RefViz, an automated clustering software for analysis of text found in title and abstract of references (Thompson ResearchSoft). RefViz is based on OmniViz, which is a powerful clustering tool used for microarray data analysis; http://www.omniviz.com/). A manual screening was also conducted to eliminate any references that were not expected to contain data related to detection limit. Approximately 100 references that were more closely related to method development or validation were chosen for further analysis. The references were categorized according to the type of method including plating, real time polymerase chain reaction (PCR), PCR, PCR followed by microarrays biosensors, immunoassay, electrochemiluminiscence, Raman spectrometry, mass spectrometry, and the type of matrix they were developed for (water, air, soil, other). Not all methods were used in all types of matrices. For some methods, sonly limited studies were found. Extraction of detection limit and normalization to the same units was the next step.

Quantum dots (QDs) as surrogates: QDs (of CdSe/ZnS/PbS) with varying properties are available commercially for various applications. Names and characteristics vary, e.g., from Evident Technologies (http://www.evidenttech.com/), it is: EviFluor, EviDot, EviDust, EviComposites etc. The last two may be especially useful as surrogates for air

dispersal experiments. Currently experimental evidence for use of QDs as surrogates of microorganisms is nonexistent but its potential as a surrogate, marker, or tracer in biodefense applications is well acknowledged. Because QDs are tunable and can be made visible at specific wavelengths, their use as surrogates of pathogens may have significant advantages. This is due to the complete elimination of the need for sampling and measurement. Detection limit and cost needs to be experimentally evaluated. It is also possible to tag QDs with short signature sequences of DNA (oligonucleotide; Pumera, et al., 2005). Many studies exist where modified QDs have been used to detect single nucleotide polymorphisms (Xu et al., 2003), pathogens (Hahn, et al., 2005), and toxins in a multiplex manner. But these applications are with biologically modified QDs, which may not be as useful for use as surrogates in all matrices. Encapsulation of QDs in viral capsids has also been reported recently (Edgar et al., 2006).

The MSDS for many of the QDs are available (Evident Technologies). EviTag (one of the QDs made of Cadmium Selenide and Zinc Sulfide is listed as moderately toxic in line with the known toxic effects of Zn, Cd, Se, and S. Development of QDs as surrogates has benefits that are over and above the advantages associated with the biological surrogates. It may play a significant role in answering the question "how clean is clean". In field-scale dispersion experiments, clean up of QD surrogates may be required (because of its toxic health effects), especially if it is used at high concentrations. The cutoff below which it will not pose a significant hazard needs to be determined using the available MSDSs. Use of QDs with attached DNA probes needs further evaluation to determine its usefulness.

Research Contributions this Year (how you advanced MRA, contributions and results from completed learning units; please list the numbers of the learning units, as follows:

Documenting the distribution of detection limit for *B. anthracis* in water for various methods and concluding that real time polymerase chain reaction (PCR), conventional PCR, and selected antibody based and chemiluminiscence assays are among the most sensitive detection methods is one of the main accomplishments this year. A similar analysis for air and soil is also complete with similar conclusions. However, for these two matrices, additional data is being collected to for each type of method to provide a more comprehensive frequency distribution curves in these matrices. The completed learning unit for water is submitted in the database with supporting documents. The learning units for air and soil are submitted as work in progress.

The work on evaluation of quantum dots has been initiated. It involves identification of characteristics of all types of quantum dots and theoretical evaluation of QDs for use as surrogate followed by an experimental validation of its usefulness. Initial literature review (presented in the background) suggests that it has good potential but its use as surrogate will require further evaluation and development. An “In progress” learning unit related to this task is also submitted.

Completed unit:

1. Detection limit *B. anthracis* in water: LU 631

In progress units:

1. Detection limit of all methods for *B. anthracis:* LU 425
2. Detection limit *B. anthracis* in air: LU 740
3. Detection limit *B. anthracis* in soil: LU 742
4. Evaluating quantum dots (QDs) as surrogates: Activity is release, dispersion, and recovery of surrogates; Matrix is air, water, soil, or surfaces: LU 738

Outputs:

8.1 Students Supported and/or Graduated: One
8.2 Publications: None
8.3 Patents: None
8.4 Presentations: One
8.5 Participation or organization of workshops: One
8.6 Case studies, algorithms developed: None
8.7 Human Resource Development: None
8.9 Other (consulting, interviews, etc.): None
8.10 Funds Leveraged (additional funding, resources for free): EPA STAR Grant: $600,000; 21st Century Grant from Michigan Economic Development Corporation: $966,608.

Outcomes (how your contributions can be used to better society): Knowledge of detection limit help quantify the risk.

Knowledge of detection limit of various available methods is key to the quantification of risk. Availability of surrogates that mimic transport and dispersion of pathogens without the associated harmful health effects improves the ability to minimize risk.

Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

Actual work in collaboration with other PIs within CAMRA is planned in November 2006 (with Dr. Chris Choi). Tracer experiments at the Water Village (at University of Arizona) are planned that will evaluate the transport of spiked surrogates in a pilot scale water distribution system. Methods identified through the exercise related to detection methods and surrogates will be used in these experiments.

Integration with other projects (association between units in different projects):

The outcome of Unit 631 will be used to develop algorithms that will relate detection limit to microbial risk (with team members of Drs. Joan Rose and Charles Haas).

Tasks for Next Year (see definition below):

In addition to completing the four learning units listed above as “In progress”, the following thee main tasks are planned for Year 2.

Document the distribution of detection limit and other parameters that influence the algorithm for quantifying risk for all BACs.

Develop an algorithm that employs the information related to detection limit with microbial risk. As shown by the distribution of detection limit of *B. anthracis* in water (Figure XX), selecting a given method to detect the presence or absence of a pathogen may have significant influence on the quantification of risk. The large variability in detection limit within a given method is also equally important. These factors will be statistically quantified and the resulting algorithm will be added to the existing microbial risk assessment toolbox.

We also plan to experimentally evaluate the performance of selected QDs as surrogates under laboratory and field conditions (e.g., in Water Village). The obvious candidates for this task are EviDust and EviComposites but cost, safety, and measurement technique will determine the final choice.

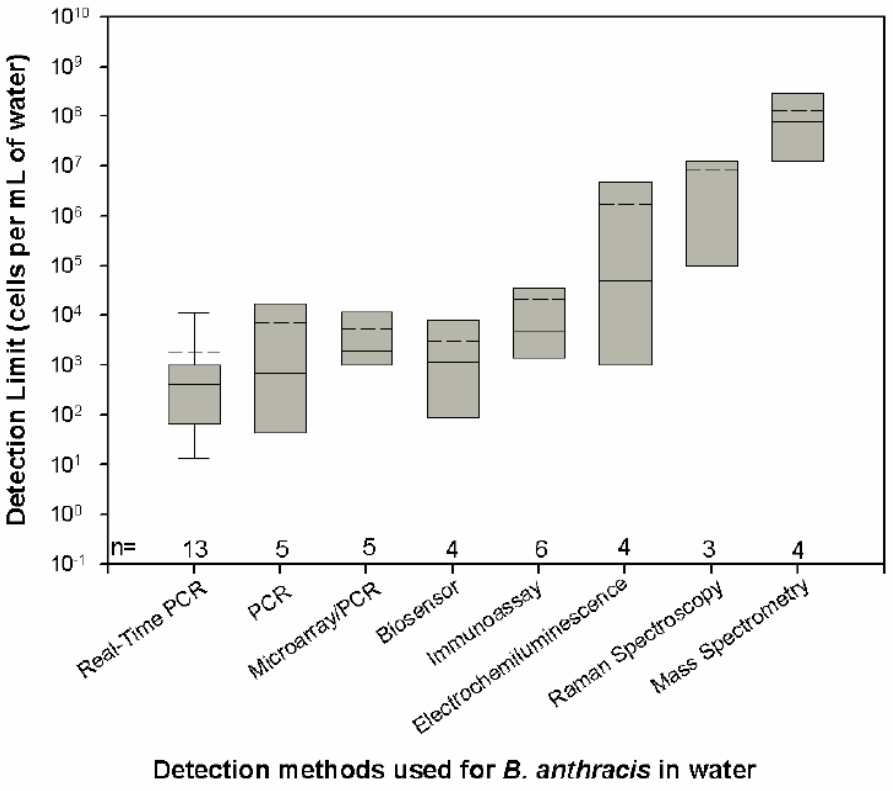

Figure XX. Distribution of detection limit for various methods available to detect *B. anthracis* in water. Solid line represents the median and dashed line represents the mean for the corresponding method. The number of studies included for each method is represented by ***n*** on the x-axis.

Anticipated Technical Results and Developments (examples of potential learning units for next year, within possible also include potential outcomes):

Evaluating detection methods for BACs

Developing an algorithm to relate detection limit to microbial risk

Experimentally evaluating selected quantum dots as surrogates under laboratory conditions

- **Tasks** are collections of research questions, problems, or hypothesis whose developments (contributions) may be described as learning units.

References

Edgar R, McKinstry M, Hwang J, Oppenheim AB, Fekete RA, Giulian G, Merril C, Nagashima K, Adhya S. (2006). High-sensitivity bacterial detection using biotin-tagged phage and quantum-dot nanocomplexes. *Proceedings of the National Academy of Sciences of the United States of America* 103 (13): 4841-4845.

Hahn MA, Tabb JS, Krauss TD. (2005). Detection of single bacterial pathogens with semiconductor quantum dots. *Analytical Chemistry* 77 (15): 4861-4869.

Pumera M, Castaneda MT, Pividori MI, Eritja R, Merkoci A, Alegret S. (2005). Magnetically trigged direct electrochemical detection of DNA hybridization using Au-67 quantum dot as electrical tracer. *Langmuir* 21 (21): 9625-9629.

Xu HX, Sha MY, Wong EY, Uphoff J, Xu YH, Treadway JA, Truong A, O'Brien E, Asquith S, Stubbins M, Spurr NK, Lai EH, Mahoney W. (2003). Multiplexed SNP genotyping using the Qbead (TM) system: a quantum dot-encoded microsphere-based assay. *Nucleic Acids Research* 31 (8): Art. No. e43.

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

Investigators: Joseph Eisenberg and James Koopman

Project Goals (from proposal, additional goals): i) Transmission Model Development; ii) Intra- and Inter-venue transmission of pathogens

Tasks* for Year (I): i) Characterize environmental data relevant for the development of environmental components of a disease transmission model; ii) Develop appropriate dynamic transmission models that include spatially explicit details of infection spread through populations and the environment; ii) Develop criteria for collapsing population-level transmission models to individual-level static models; iii) Establish classification criteria for venues; iv) Establish intra-venue models for each venue class; v) Make preliminary assessment of what best inform the conformation of the models

Research Activities (First field in learning units, starts w/ verb in -ing form, e.g., investigating):

A. Creating the database structure to organize data relevant to transmission systems modeling.

B. Randomized influenza intervention trial study design (Determining the effects of two non-pharmacological interventions on environmental mediators of infection transmission).

C. Environmental model development of single objects (Modeling the temporal patterns of contamination on a single abstract surface).

D. Environmental model development of single venue (Modeling dissemination of

pathogens in a single venue explicitly incorporating human behavior)

E. Environmental transmission model development of multiple venues (Modeling

transmission and dissemination of pathogens in and between multiple venues)

F. Influenza transmission model on a college campus (Modeling transmission using data collected from randomized trial)

G. Relaxing the assumption of symmetric contact within transmission models (Developing models with asymmetric contact)

Background and prior research (from learning units of the type Things I have read, those essential references you want to include; from Year II, include summary of previous years):

We have not entered any LU under the category type "Things I have read". We will begin to enter these units soon.

Research Contributions this Year (how you advanced MRA, contributions and results from completed learning units; please list the numbers of the learning units, as follows:

A. We have designed a relational database (in Microsoft Access) that structure pathogens by characteristics. This database will be collaboratively filled as relevant data is gathered from the literature and colleagues. The structure of the database contains information relevant to transmission: i) Natural history of infection and immunity; ii) Environmental survivability; iii) Transfer coefficients; iv) Dose-response. We defined an organizational scheme for parameters relevant to transmission processes. This defines the scope of the literature required for parameterization of our population transmission models, and thereby aids us in the identification of research needs; i.e., it identifies those process parameters that are not found in the literature and not being pursued by CAMRA investigators. This database structure can ultimately become a means for an alternative taxonomic classification of infectious pathogens. (completed LU #)

B. We are collaborating on a randomized influenza trial assessing the causal effects of two non-pharmacologic interventions. Groups will be randomized into three arms: i) no intervention, ii) only wearing mask, and iii) wearing mask and alcohol hand-washing. Each group is a different set of University of Michigan dormitories. Samples will be collected from students and the environment after the first identification of influenza. In addition, we will conduct surveys of exposure behaviors both within and outside dormitories to estimate contact patterns. This is a two-year project where a goal of the first year is to inform the experimental design of the second year. The goal of this project is to understand how much influenza transmission results from fomite vs. airborne routes. Another goal is to estimate how much are these routes diminished by each intervention. To obtain these goals we plan on collecting data to: 1) characterize the magnitude and distribution of environmental contamination in each trial arm; and 2) describe the symptomatic infection frequency in each trial arm. The symptomatic infection frequency together with the environmental data and our transmission models will provide a better estimate of the true causal effect of each intervention arm. (in progress LU #)

C. We are interested in understanding how to customize sampling strategies on specific surfaces. Different materials or different surfaces might require different sampling strategies in order to obtain an accurate measurement of the contamination. Our premise is that sampling strategies depend on the temporal patterns of contamination. These

temporal patterns of contamination are a function of the characteristics of the surface, the frequency at which people touch the surface, and the contamination level within the population. We are describing this process through a model. Specifically, we model the contamination dynamics on a single abstract surface takes into account: 1) Number of touches per unit time; 2) proportion of people contaminated; 3) mean contamination level on an individual; 4) standard deviation of the contamination level on an individual; 5) proportion of contamination deposited on surface per touch event; 6) proportion of contamination picked up on surface per touch event; 7) Inactivation rate. (in progress LU #646)

D. We created a model of contamination within a single venue to better understand how both environmental conditions and human behavior affect the fate and transport of contamination. This can be used as a tool to develop decontamination strategies. Our eventual goal is to understanding pathogen dissemination and transmission within a single venue. This has also helped in the development of our multi-venue models that are concerned with both within venue transmission and between venue dissemination. In the single venue model people enter via a Poisson process and leave with some constant probability. Within the venue, people move to random locations on a two-dimensional grid. They deterministically deposit and/or pickup contamination to/from the environment. Even under these idealized conditions, which minimize the complexity of the contamination process in the environment, contamination dynamics are still very complicated. One reason for these complicated dynamics is that there is a delay created when human behavior is included in the model. Sampling usually assumes a rapid convergence to equilibrium, as found in continuous compartmental models. However, our results show that convergence depends on the characteristics of the system, and usually it is orders of magnitude larger. This would imply that sampling should take into account the stochastic fluctuations out of equilibrium, which is not the current standard. (In progress LU #504)

E. We built a multiple venue model. The model components include pathogens, people and the environment. Transmission occurs when people contaminate the environment with pathogens and when susceptible people pickup this contamination. The model's dynamics are affected by venue characteristics, venue connectivity, pathogen

characteristics, human characteristics, and human behavior. Multiple modes of transmission through the environment, currently fomites and air, are explicitly modeled. Based on our preliminary findings our model agrees with previous findings that suggest that connectivity between venues has an effect in the overall transmission system by primarily affecting the pattern of dissemination between venues. (in progress LU #)

F. To effectively model influenza transmission in a college campus requires a structure that can capture the important environmental and transmission process while maximizing parsimony. To achieve this aim, we are currently conceptualizing how to best integrate what we have learned in the above three model structures developed to date: environmental models of single objects; environmental models of single venues that incorporate multiple objects; and environmental models of multiple venues. We are further conceptualizing how best to integrate the data that will be collected in the intervention trial into our transmission model. (in progress LU #)

G. We are continually trying to understand ways to simplify transmission models. One potentially important property of our environmental transmission model is asymmetric contact. We would like to explore the importance of preserving this asymmetry in simpler model structures. (Have not entered this in as a LU)

Outputs:

8.1 Students Supported and/or Graduated: Ian Spicknall (PhD student), Sheng Li (PhD student), Josep M. Pujol (post-doc)

8.2 Publications: None
8.3 Patents: None
8.4 Presentations:

Sheng Li & Ian Spicknall, "Risk Assessment for Biosecurity", Doctoral Program Day Poster Session, University of Michigan, Mar. 2006, First Place Award.

Assessing Infection Risks and Control Options when Transmission is Person-to-Person via Multiple Routes across Diverse Venues: Jim Koopman, Joe Eisenberg, Sheng Li, Ian Spicknall University of Michigan To be presented at the Society for Risk Analysis, Dec. 5

8.5 Participation or organization of workshops:
8.6 Case studies, algorithms developed:

To conduct our research we developed several individual-based and agent-based computational models. In particular:

i) Model of contamination on single objects (research activity C)
ii) Model of transmission in single venues (research activity D)
iii) Model of transmission in multiple venues (research activity E)

These model are written in JAVA using the REPAST library. The scope of those models is mainly to fit our research agenda. However, other researcher within or outside CAMRA could also benefit from those models either extending them or using to test other hypothesis.

8.7 Human Resource Development:
8.9 Other (consulting, interviews, etc.):
8.10 Funds Leveraged (additional funding, resources for free):

Dr. Koopman will be collaborating in the Center of Excellence in Public Health Informatics directed from the University of Utah, headed by Matt Samore, and funded by CDC. The student to be supported will be integrated into our CAMRA team.

Outcomes (how your contributions can be used to better society):

A. We aim to identify relevant parameters of the transmission process in order to build more accurate and realistic models to support QMRA decision making.

B. We aim to answer the following questions: How much influenza transmission is via fomite or airborne routes. Also, how much are these routes diminished by each intervention (nothing, masks and alcohol hand-washing).

C. We aim to inform single object environmental sampling strategies through model simulations.

D. We aim to inform single venue environmental sampling through model simulation, and ultimately inform decontamination control strategies.

E. Compared to more conventional single venue models multiple venue models take into account the connectivity patterns between venues allowing us to examine more sophisticated control strategies.

F. This influenza model will help determine the relative contributions of air vs. fomite transmission in the data collected from the intervention trial as well as aiding in estimating the causal effect of handwashing and mask wearing interventions.

G. Simpler models will be easier to use and interpret.

Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

A. We have collaborated with Project I to obtain data and to talk about future experiments and data collection activities. We have just begun to collaborate with Project III about relating static dose response relationships with dynamic transmission rate parameters.

B. We are collaborating with an outside research group that obtained CDC funds for the intervention trial to augment their study with environmental sampling, surveys on student movement patterns, and transmission models.

Integration with other projects (association between units in different projects):

Tasks for Next Year (see definition below):

A. Continue to fill in the database and summarize data needs

B. Complete year 1 analysis of data and redesign year 2 intervention study

C. Complete and publish single object model with advice on sampling strategies

D. Development of single venue intervention scenarios using single venue model.

E. Development of multiple venue intervention scenarios using the multiple venue model. Test the multiple venue model using outbreak data.

F. Complete the influenza model at the college campus level and use to help redesign intervention study.

Anticipated Technical Results and Developments (examples of potential learning units for next year, within possible also include potential outcomes):

* **Tasks** are collections of research questions, problems, or hypothesis whose developments (contributions) may be described as learning units.

Project: Project III Dose Response Models

Investigators: Dr. Charles N. Haas (PI), Mark H. Weir (RA), Sushil Tamrakar (RA)

Project Goals (from proposal, additional goals): To develop dose-response relationships and models for biological agents of concern that can be transmitted via inhalation or other routes of exposure

Tasks* for Year (I): Assemble a bibliography of dose response data for category A bioterrorism agents of interest. Then fit existing dose response models to the data thereby assembled.

Research Activities (First field in learning units, starts w/ verb in -ing form, e.g., investigating): Data mining and determining the best fitting models of data for *Bacillus anthracis, Variola major, Pasturella pestis* and viral hemorrhagic fevers, then continuing to remaining category A bioterrorism agents of interest.

Background and prior research (from learning units of the type Things I have read, those essential references you want to include; from Year II, include summary of previous years):

Research Contributions this Year (how you advanced MRA, contributions and results from completed learning units; please list the numbers of the learning units, as follows: We have shown that the inhalation data sets for infection (mortality) of monkeys by *B. anthracis* spores can be pooled with the data sets obtained in guinea pigs to get a single combined dose-response model. We have determined best fit parameters for this model and also confidence distributions via bootstrapping. This is described further in the learning unit titled ‘Dose Response Model Fitting for Inhalation of *Bacillus anthracis* Spores in Different Host Species’. A paper on this is in preparation. These analyses were done using a program developed in the R language (and validated against prior data sets of the PI).

We have also started the assembly of bibliographies on Variola (smallpox) and the category A hemorrhagic fever viruses.

An MS thesis has been almost completed (final draft presently under review) which

summarizes the data on subcutaneous infection of animals by Yersinia pestis (plague). This is described in the "things that are in progress" and "things I have completed" learning units titled 'Fitting dose response models to Yersinia pestis (Y. pestis) dosing data for; wild caught squirrels and lab reared rock squirrels via subcutaneous inoculation'.

in progress unit: Dose response model fitting for inhalation of *Bacillus anthracis* spores in different host species,
completed unit: Dose response model fitting for inhalation of *Bacillus anthracis* spores in different host species
in progress unit: Fitting dose response models to *Yersinia pestis* (Y. pestis) dosing data for; wild caught squirrels and lab reared rock squirrels via subcutaneous inoculation , completed unit: Fitting dose response models to *Yersinia pestis* (Y. pestis) dosing data for; wild caught squirrels and lab reared rock squirrels via subcutaneous inoculation
In progress unit: Dose response model fitting for exposure to *Variola major* and *Variola minor* in different host species (will include data bibliography references)
In progress unit: Dose response model fitting for exposure to hemorrhagic fevers in different (will include data bibliography references)

Outputs:

8.1 Students Supported and/or Graduated: Mark H. Weir (PhD student), Sushil Tamrakar (PhD student, started September 2006). Bishel Kurungattu (unsupported MS student, completion of thesis anticipated by December 2006).

8.2 Publications:

8.3 Patents:

8.4 Presentations: **Effect of Host Species on the Dose Response of Inhaled *Bacillus anthracis* spores.** Accepted for a podium presentation at the Society of Risk Assessment Annual Meeting December 3-6, 2006 Baltimore, Maryland

8.5 Participation or organization of workshops:

8.6 Case studies, algorithms developed:

1. R source code for maximum likelihood estimation approach for parameter estimation of dose response models.
2. R source code for bootstrap analysis for development of confidence intervals for risk projection.

8.7 Human Resource Development:

8.9 Other (consulting, interviews, etc.):

8.10 Funds Leveraged (additional funding, resources for free):

1. Mark H. Weir E.I.T.: GANN fellowship effective starting date: Fall 2006 Term
2. Bishell Kurungattu: Unsupported Masters of Science student

Outcomes (how your contributions can be used to better society):

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.

Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

Integration with other projects (association between units in different projects):

Tasks for Next Year (see definition below):

Development of dose-response information for exposure to Variola (smallpox)
Development of dose-response information for exposure to hemorrhagic viruses (e.g., Lassa, Marburg, Ebola)

Development of novel dose-response models incorporating time to infection and physiological parameters

Review of outbreak studies for validation data sets

Anticipated Technical Results and Developments (examples of potential learning units for next year, within possible also include potential outcomes): Further use and verification of R source codes to describe category A agents of interest with best fitting dose response models, and develop an understanding of the risk associated with these microorganisms. This will then likely move on to category B agents of interest and to eventually develop a library for the best fitting models and their associated optimized parameters.

* **Tasks** are collections of research questions, problems, or hypotheses whose developments (contributions) may be described as learning units.

Haas, C.N., 2002. On the risk of mortality to primates exposed to anthrax spores. *Risk Analysis*, 22:2:189.

Project: IV (Drexel Portion)

Investigators: Patrick Gurian

Project Goals (from proposal, additional goals):

Develop decision models for two scenarios. Quantitatively model one scenario using probabilistic techniques to describe uncertainty. Identify key decision making points for both public and risk managers. Identify key uncertainties for future research efforts.

Tasks* for Year (I):

A) Identify and describe priority scenarios.

B) Work with CMU to identify key behavioral components of these scenarios and important topics for semi-structured interviews.

C) Model a small-scale, indoor anthrax release.

D) Develop a Bayesian hierarchical model of anthrax dose-response in different species.

Research Activities (First field in learning units, starts w/ verb in -ing form, e.g., investigating):

Developing compartment model of anthrax fate and transport in the indoor environment.

Fitting of a Bayesian hierarchical dose-response model for anthrax.

Identifying model parameters from a literature review.

Discussing appropriate scenarios and behavioral aspects of those scenarios with CMU.

Background and prior research (from learning units of the type Things I have read, those essential references you want to include; from Year II, include summary of previous years):

Sextro and co-authors have conducted compartment modeling of anthrax exposure. This work provides valuable information on deposition and re-suspension rates but does not assess the importance of different model uncertainties nor does it develop threshold surface concentrations for response decision making.

Research Contributions this Year (how you advanced MRA, contributions and results from completed learning units; please list the numbers of the learning units, as follows:

Surface concentration of anthrax corresponding to a risk of 1/1 million have been calculated. These are demonstration calculations to show how sampling might be quantitatively linked to risk levels.

A Bayesian hierarchical model of anthrax dose response has been fit. This will inform efforts to use surrogate species to predict dose-response to microbial agents.

Outputs:

8.1 Students Supported and/or Graduated:

Ashley Kenyon, M.S. student, graduated in June 2006.

8.2 Publications:

A student report has been written describing the calculation of the surface concentrations for anthrax corresponding to 1/1 million risk. This will inform our presentation to SRA but will require further work before it is ready for submission to a journal.

8.3 Patents:

8.4 Presentations:

"Responding to anthrax contamination: Listening to surfaces and talking to people," Gurian, Dudley Ward, and Kenyon, accepted for presentation at the annual meeting of the Society for Risk Analysis, December 2006.

8.5 Participation or organization of workshops:

Organized a symposium titled "Building on Microbial Risk Assessment to Address Bioterrorism" scheduled for the annual meeting of the Society for Risk Analysis in Baltimore in December.

8.6 Case studies, algorithms developed:

The project has developed a scenario for an anthrax release.

A simple algorithm has been developed which uses a Bayesian approach to assessing residual risk of contamination after surface sampling. The use of a discrete approximation to a log-uniform distribution as a prior allows posterior risk to be computed easily using a closed-form solution that can be implemented in a spreadsheet.

8.7 Human Resource Development:

Providing support to two graduate students, Nicholas Dudley Ward (M.S. ongoing) and Ashley Kenyon (M.S. completed)

8.9 Other (consulting, interviews, etc.):

8.10 Funds Leveraged (additional funding, resources for free):

Jade Blackwood has obtained funding for the academic year through the GEM foundation. She will begin work on the project as soon as her M.S. thesis is complete.

Outcomes (how your contributions can be used to better society):

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 1) guidance for regulators as they seek to develop response plans and 2) priorities for research to reduce key uncertainties.

Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

An email discussion among Gurian, Casman, and Downs is in progress to identify the key elements of the semi-structured interviews.

Integration with other projects (association between units in different projects):

Patrick Gurian visited with Ian Pepper, Chris Choi and his students, and members of Chuck Gerba's lab in Arizona in April. Risk management of a water scenario was identified as a possible point of collaboration. While considering an additional scenario would expand the work done by Project IV, this additional scope may be feasible if Chris Choi's students are able to work on the scenario.

Project IV held a meeting in Pittsburgh in July. Mitchell Small, Patrick Gurian, Liz Casman, and Julie Downs were all in attendance. Household preparedness was identified as a possible focus of the semi-structured interviews as it is an import behavioral issue that impacts risk.

Tasks for Next Year (see definition below):

The results of the Bayesian hierarchical dose-response modeling for anthrax will be compared with the classical dose-response models fit by Project III.

The existing compartment modeling of anthrax will be expanded into a system of coupled indoor-outdoor models with a re-suspension component, including simplified removal factors for HVAC filters and coils. Software for this will be developed in Matlab. Surface threshold concentrations will be computed for this scenario. Surface concentrations will be evaluated as indicators both of past exposure and of future exposure. An effort will be made to try to identify those surfaces that are relatively insensitive to model uncertainties (i.e. those that are closely correlated with risk, regardless of specific uncertainty and variability). Both Bayesian and classical approaches will be considered to assess residual risk and compute required sampling areas to certify a site as clean. A presentation at SRA will summarize initial results in December and a journal submission will be prepared by end of January.

Water scenarios will be explored with Chris Choi of Project I and his students.

Anticipated Technical Results and Developments (examples of potential learning units for next year, within possible also include potential outcomes):

The merits of Bayesian hierarchical models as descriptions of the effects of anthrax on different species will be assessed.

Surface sampling approaches and target areas will be identified. Bayesian and classical approaches to defining “clean” will be contrasted.

Key uncertainties in understanding large-scale anthrax releases will be identified. Future work will then assess the extent to which these uncertainties are likely to be amenable to reduction through research.

* **Tasks** are collections of research questions, problems, or hypothesis whose developments (contributions) may be described as learning units.

Project: 4 (CMU part)

2. Investigators: Casman, Downs, Small, Gurian

3. Project Goals:

- Understanding how the public's perception of bioterrorism risks affects their behavior and abilities to effectively manage their personal risks
- Assembling quantitative estimates from the published literature of behaviors observed and attitudes expressed concerning risk reduction in epidemic or bioterror scenarios.

4. Tasks* for Year (I):

- Develop method for anticipating neglected needs for public risk-related communications using risk analytic techniques
- Provide plague briefing document to support short-lead-time risk-communications development
- Assemble published quantitative estimates of risk-mitigating behaviors that would affect the outcomes of bioterrorism simulation models
- Choose two scenarios for mental models interviews.
- Begin developing interview protocol.

5. Research Activities (First field in learning units, starts w/ verb in -ing form, e.g., investigating):

- Compiling results of survey work on risk-mitigating behaviors in epidemic/bioterror settings. LU Title: Review of studies documenting behaviors or expressed willingness to comply with recommendations influencing personal risks during epidemics and bioterrorism events (1)
- Constructing influence diagram (expert model) for plague risk scenario
- Developing support document for influence diagram
- Identifying affected population sectors
- Identifying critical decisions and choices LU Title for preceding 4 bullets: Plague scenario development. (2)
- Identifying opportunities/needs for risk communications LU Title: Planning plague risk communication content. (3)

- Using diagram and document to demonstrate a novel risk communication planning method. LU Title: Demonstration of an integrated assessment-inspired communications planning tool (4)
- Internal CAMRA a review of expert model
- Selecting second terrorism scenario
- Designing interview protocol: LU Title: Designing mental models interview concerning public perception of bioterrorism risk mitigation choices. (5)

6. Background and prior research (from learning units of the type Things I have read, those essential references you want to include; from Year II, include summary of previous years):

LU 1 (Review of studies documenting behaviors or expressed willingness to comply with recommendations influencing personal risks during epidemics and bioterrorism events) This LU is in the form of an attached document. A KR notice has been sent to the PIs of project 2 so they can look it over and see if they can use anything for their model development. We in project 4 are of course also using it to guide our work. My guess it is 80% complete.

7. Research Contributions this Year (how you advanced MRA, contributions and results from completed learning units; please list the numbers of the learning units, as follows:

LU 1 is in progress, but getting pretty complete.

LU 2 is complete.

LU 3 is complete

LU 4 is complete, well, still a draft paper, but has gotten some internal CAMRA review (M. Wagner) and internal CMU review. 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. Since the situation could be quite complex and mutable, it is possible that other needs would arise. A briefing document that could serve as a quick reference for those questions is also a product of this work. Doing this kind of preparation for other bioterrorism scenarios could prevent embarrassing gaffs, like when T. Thompson speculated that the Amerithrax index case contracted his infection by drinking from a stream.

LU 5 is in progress

Outputs:

8.1 Students Supported and/or Graduated: none
8.2 Publications: a draft paper
8.3 Patents: none
8.4 Presentations: Going to present at SRA annual meeting
8.5 Participation or organization of workshops: CAMRA summer school lecturer
8.6 Case studies, algorithms developed: urban plague zoonosis
8.7 Human Resource Development: ?
8.9 Other (consulting, interviews, etc.): none
8.10 Funds Leveraged (additional funding, resources for free): CAMRA got $70K from CREATE (v Winterfeldt) for survey development. Also CREATE (Lave) is interested in the influence diagram approach for structuring economic analysis of terror events (paying 1 month of my CMU salary). We are using funds from the MacArthur Fdn to support a grad student to parameterize the zoonotic portion of the plague model to determine if urban ecosystems could support plague transmission. (Durham) $65K/yr.

9. Outcomes (how your contributions can be used to better society):

Developed 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.

10. Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

CAMRA: Mike Wagner and Carole Bollin were asked to fact-check an early draft of the plague paper.

CREATE: Working with Lester Lave on bioterrorism economics analysis.

Working with Downs, Fischhoff, Florig & DeKay (all CMU) on exploring results from plague paper in terms of public perception (NSF funding – but not included with leveraged funds because that award pre-dated CAMRA).

11. Integration with other projects (association between units in different projects):

Someday Project 2 will notice us.

12. Tasks for Next Year (see definition below):

- Develop anthrax decontamination/reoccupation scenario and expert model
- Analyze anthrax scenario
- Develop mental models interview questions
- Obtain CMU and MSU IRB and EPA approval of protocol

- Train interviewers
- Pre-test interview protocol.
- Revise protocol.
- Conduct and transcribe interviews.
- Begin coding of interviews.

13. Anticipated Technical Results and Developments (examples of potential learning units for next year, within possible also include potential outcomes):

Anticipated LUs

- Anthrax scenario development.
- Anthrax risk communications analysis
- Mental models interview protocol
- Coded results of mental models interviews.

* **Tasks** are collections of research questions, problems, or hypothesis whose developments (contributions) may be described as learning units.

1. Project: V (Weber, Atwood, Han)

2. Investigators: Rosina Weber (PI), Michael Atwood (Co-Investigator), Hyoil Han (Co-Investigator), Jason M. Proctor (funded RA), Marcia Morelli (unfunded doctoral student)

3. Project Goals (from proposal, additional goals):

Our primary goal was to build the web-based knowledge repository to support sharing and leveraging for the CAMRA community members. The system is operations 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.
These other aspects are being studied and will be implemented in version 2.0, to be launched during Year II. After completion of version 2.0, when all maintenance aspects and variations in the learning units are finalized, we will conduct tests reasoning with learning units and the domain structure. This repository will be later associated with a data warehouse to be built in Year III.

4. Tasks for Year (I):

All tasks for Year I were fully performed.

General Tasks:

- Building Knowledge Repository for the CAMRA community.
- Introducing the CAMRA knowledge management approach to the CAMRA community.

Specific:

- Setup and hiring
- Designing knowledge repository
- Visits to Community members
- Studying learning units (50%)
- Maintenance of knowledge repository (50%)

5. Research Activities (First field in learning units, starts w/ verb in -ing form, e.g., investigating):

In this period, investigators in Project V have focused on designing and implementing the knowledge repository and visiting community members. During these visits, we were able to investigate learning units and an adequate domain structure for the QMRA domain. We have also worked on maintaining knowledge repository. There are six research activities to report:

1. Designing the knowledge repository (units 743 and 621)

2. Implementing and testing the knowledge repository (units 745 and 730)

3. Investigating learning units (units 732 and 746)

4. Investigating the domain structure for QMRA (units 733, 748)

5. Presenting CAMRA KR version 1.0 to members (734, 749)

6. Monitoring and maintaining the knowledge repository (735, 750)

6. Background and prior research (from learning units of the type Things I have read, those essential references you want to include; from Year II, include summary of previous years):

The design of the CAMRA KR repository is mostly based on previous work by Szulanski (1996), Weber et al. (2001), and Weber and Aha (2003).

7. Research Contributions this Year (how you advanced MRA, contributions and results from completed learning units; please list the numbers of the learning units, as follows:

1. Designing the knowledge repository (units 743 and 621)

When designing the CAMRA KR, we wanted to find out the adequate design of our CAMRA KR system with essential elements for knowledge sharing.

We grouped our team of experts in knowledge management, database development, requirements engineering, and human-computer interaction and started to deliver the steps for designing a web and repository -based KM system for CAMRA using learning units as its main knowledge artifact. We designed a paper prototype to discuss with CAMRA members at the Feb kickoff meeting for feedback and tailoring the design to the CAMRA community.

Contribution:

We learned how to design a system with essential elements for knowledge sharing. This design requires human-computer interaction activities.

2. Implementing and testing the knowledge repository (units 745 and 730)

When implementing and testing the knowledge repository, we wanted to find out what were the challenges and lessons we may learn from implementing and testing the knowledge repository for the CAMRA community.

After the design for entering learning units was completed, we started with the implementation. We started testing the system for entering learning units because these

have to be tailored for the community. Subsequently, we designed methods for search and other needs.

Contribution:

The changes required to the initial implementation require structural changes in the program. It is a better practice to build a prototype version and test with all the community before we understand all requirements.

Prototyping is a crucial step when tailoring a repository of knowledge artifacts to a new domain.

3. Investigating learning units (units 732 and 746)

When investigating learning units, we initially wanted to find out what were the required categories of learning units for the CAMRA KR. Are the original three types enough to cover the revised design? How about field labels?

Starting from the original three categories of learning units, knowledge facilitators introduced the system to CAMRA members and helped them associate their work with the learning unit paradigm.
Initially, there were no plans for the tool to incorporate all contents for reporting. We have to define a learning unit type for outputs and test its need and compare to the use of existing learning units to accommodate outputs, e.g. papers, presentations. Besides, we have to inquiry whether accomplishments are perceived by the funding agencies in the same level as research contributions. For example, is implementing the KR an accomplishment that is to be reported as a research contribution?

The first round of demonstrations to the users and obtaining feedback is completed. We now start designing version 2.0 that will incorporate the reporting capability for drafting reports for EPA.
We need to design the units that will accommodate all entries to support the report, including outputs. There is no correspondence between units and outputs. Are outputs another type of learning unit or should the design incorporate another type of record for outputs?
We will now revise the design, evaluating these alternatives.

We are currently trying to find out whether should we add a fourth type of LU for accomplishments? What should the labels be in this new type?

4. Investigating the domain structure for QMRA (units 733, 748)

When investigating domain structure, we wanted to find out what is the general form of the QMRA domain that is consistent with CAMRA members view?

We asked all users to represent on paper how they envisioned the domain of CAMRA. The representations are being analyzed to create a complete and consistent structure of the domain that does not conflict with any member's idea of the domain.

In addition, we are investigating the use of visualization tools to produce visual representations from learning units. Figure 1 shows an example of how keywords are distributed in the current universe of learning units. We will later build a comprehensive map using rese

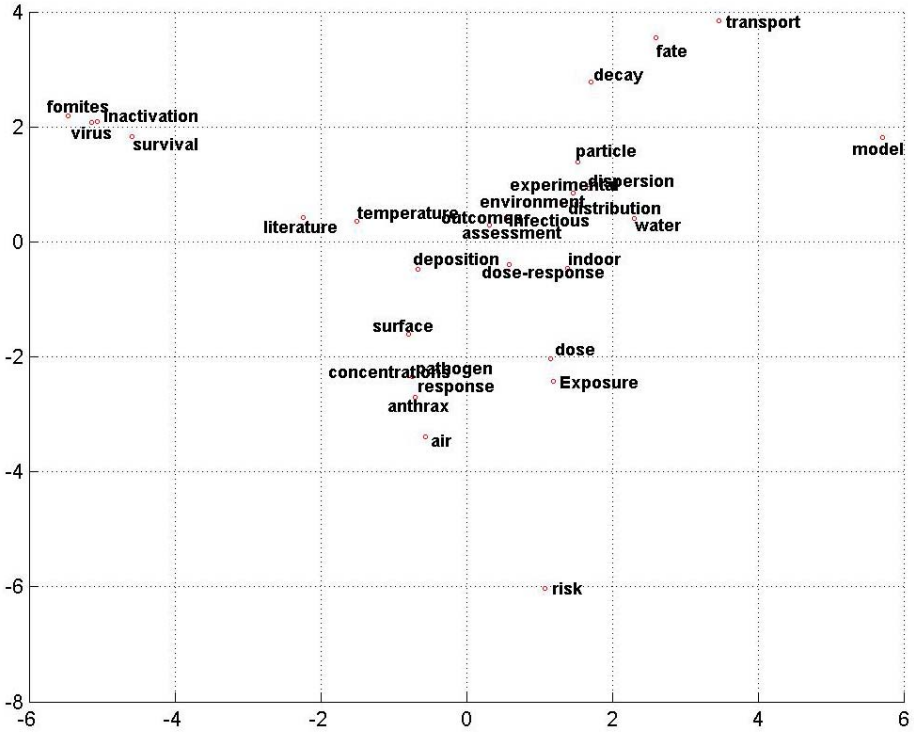

Figure 1

In Figure 2, an example of how investigators can be organized within (a) and across projects (b). Please note that not all members were registered when these networks were created.

When investigating domain structure with information science, we wanted to find out whether bibliometrics methods can help us determine an adequate domain structure for the QMRA domain?

We followed the steps:

Step 1: Identifying Contextual Core Authors in the Subfields Using Iterative Chaining
Step 2: Combining the Parent Fields' Characterizations

The results are in press in the paper: Proctor, J. M., & Weber, R. (2006). Identifying the Core of an Emerging Multidisciplinary Domain. In Proceedings of the ASIS&T 2006 Annual Meeting (in press).

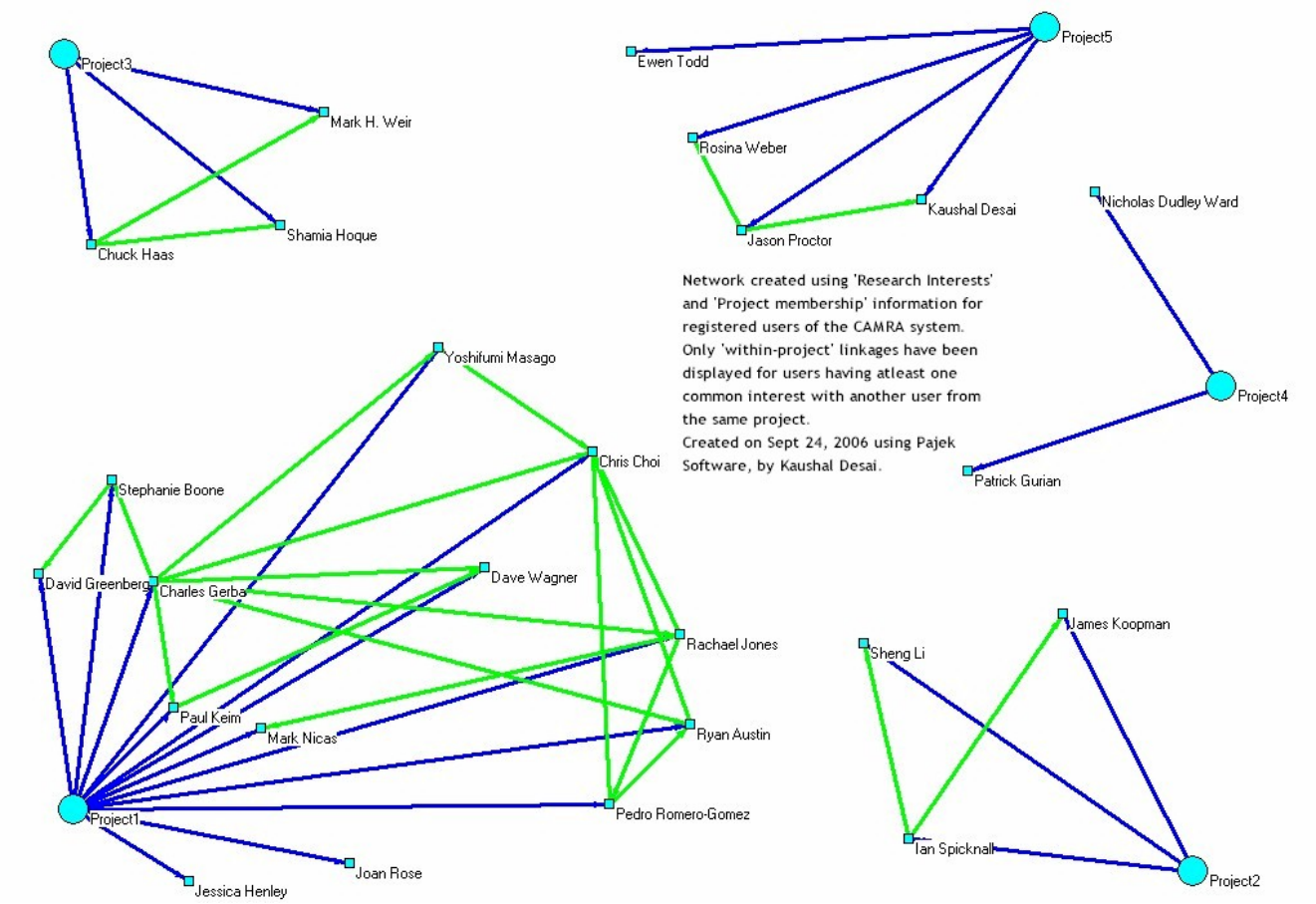

Figure 2 (a)

5. Presenting CAMRA KR version 1.0 to members (734, 749)

When presenting CAMRA KR to members, we wanted to find out how would CAMRA members receive the CAMRA KR?

Members of Project V visited all CAMRA sites introducing the CAMRA KR and explaining it in the context of the knowledge management approach designed for knowledge sharing, collaboration, and integration. Visits started on July 20, 2006.

Contribution:

See below table describing visits. Slides shown to members during visits can be made available.

CAMRA members allocated required time to be introduced to the system. All members have entered units during visits. They all asked questions providing invaluable feedback. It was observed in all visits that members showed interest in reading and becoming acquainted with their colleague's work.

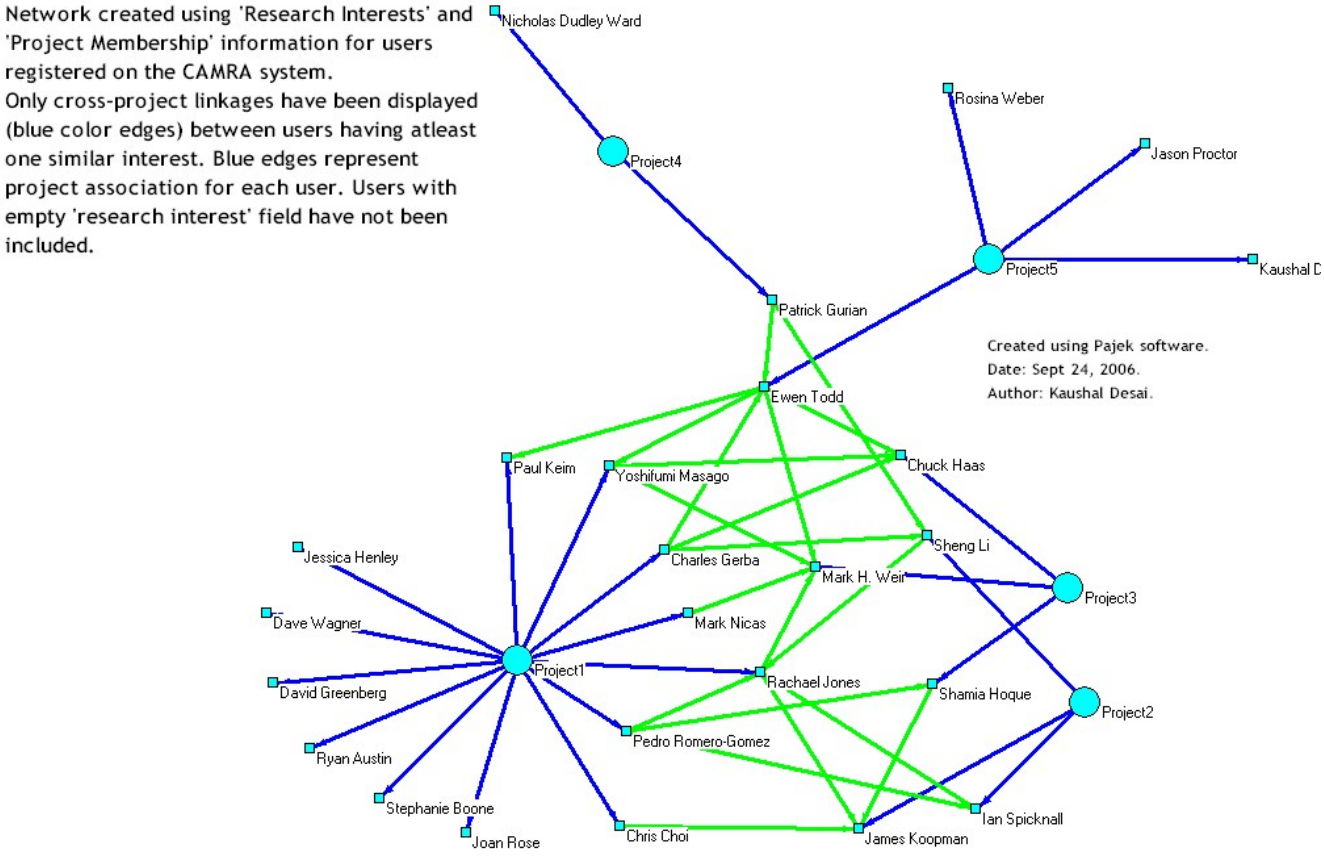

Figure 2 (b)

6. Monitoring and maintaining the knowledge repository (735, 750)

When monitoring and maintaining the knowledge repository, we initially wanted to determine a stable set of methods that guarantee the quality and preservation of the repository.

We are monitoring the use of the repository through the submission-approval process. We are identifying design flaws that may cause a unit to be lost. We have established a daily backup routine so that all units stored by some time everyday are copied to a backup. We are purchasing the new server to store the repository and we will store backups in a different building. For the quality of the stored data, we are examining the occurrences of research activities and contexts to implement drop down lists in version 2.0.

We are trying to determine a stable set of methods that guarantee the quality and preservation of the repository.

We will design a new process to allow contributors to make edits in the four core fields. The process will incorporate a 'graveyard' for replaced units.

Evaluation:
As an annual performance measure (APM) for Project V, we propose, “Knowledge Repository to promote and facilitate knowledge sharing, collaboration, and integration of CAMRA consortium participants".
The evaluation of this performance measure is not yet possible following any rigorous method. However, there are evidences that suggest that, at the present level of version 1.0, this performance measure has been met.
The promotion of knowledge sharing, collaboration, and integration was undertaken during the visits with all members. We explained how knowledge sharing, collaboration, and integration are required for a consortium and that our knowledge management (KM) approach had these three goals. Knowledge sharing, collaboration, and integration are motivated as we explain, invite, and motivate members to submit learning units describing their work. Collaboration is motivated in the system in different ways. First, as members see units submitted by other members under “Find Units”. Then, when entering a learning unit, contributors are invited to identify members they would like to notify about the submission of the new unit. The following step in the system is to associate learning units. The member entering a unit is asked to associate the new unit to existing ones. When they associate a new unit with an existing unit authored by a different contributor, he or she is asked to explain the nature of the association. This requirement forces the contributor to understand the unit to be associated in depth before claiming an

association exists. Members are oriented by knowledge facilitators to seek for associations that require their expertise to be recognized and explained. If the member who describes the association did not know about the existing unit before that session, then the assumption is that knowledge sharing took place, i.e., knowledge from the existing unit was transferred to the contributor of the new unit. However, it is possible that this member has heard about the work on the existing unit by other means, preventing us from concluding knowledge sharing from the association. Thus, for version 2.0, we plan to ask members whether the association step caused knowledge to be shared.

Outputs:

8.1 Students Supported and/or Graduated:

Jason M. Proctor was supported with stipend and tuition.

8.2 Publications:

1. Weber, R. O., Morelli, M. L., Atwood, M. E. & Proctor, J. M. Designing a Knowledge Management Approach for the CAMRA Community of Science. Accepted for presentation at PAKM 2006 (Practical Aspects in Knowledge Management).

2, Proctor, J. M., & Weber, R. (2006). Identifying the Core of an Emerging Multidisciplinary Domain. In Proceedings of the ASIS&T 2006 Annual Meeting (in press).

8.3 Patents:

8.4 Presentations:

QMRA Summer Institute at Michigan State University. East Lansing, Michigan, 08/06/06. Topic: Introduction to Knowledge Management @ CAMRA.

8.5 Participation or organization of workshops:

Not directly related, R. Weber co organized a workshop with Hüllermeier, Eyke and Richter, Michael on Uncertainty and Fuzziness in Case-Based Reasoning as part of the Workshop Program at the European Conference on Case-Based Reasoning 2006.

8.6 Case studies, algorithms developed:

Publication number 2 describes an algorithm for identifying core publications and core authors in an emerging domain. An emerging domain is one that is not established yet, it is new and typically composed of researchers from multi-disciplinary fields of study.

8.7 Human Resource Development: Doctoral student J. Proctor attended the QMRA summer institute where he was introduced to the field of QMRA.

8.9 Other (consulting, interviews, etc.):

Interview with Bridge Magazine on June 6, 2006. This interview is the cover of the Fall 2006 issue (http://www.cis.drexel.edu/Home/About/pubs/).

8.10 Funds Leveraged:

The tuition for J. Proctor was paid through cost sharing by Drexel University.

Marcia Morelli has worked for the whole year in the design of the CAMRA KR as a research experience, so no funds were spent on her contribution. She is a doctoral student and expert in human-computer interaction. She is the second author of one of our publications.

Two other doctoral students have joined Project V to work for research experience. Kaushal Desai started in the summer to investigate visualization tools. Sidath Gunawardena joined us in September and he is investigating the design of reporting methods.

8. Outcomes:

Our 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."

9. Collaboration with other Projects (actual work in collaboration within and outside CAMRA):

Many learning units were conceptualized and submitted in collaboration between members of Project V and members of other projects. These collaborations took place during the visits. The visits occurred as follows:

Institution visited	Project visited	Members of project being visited	Members Project V	Dates of visit
Drexel University	Project III	Chuck Haas, Mark Weir	R. Weber, J. Proctor	July 20, 21, 25
Drexel University	Project IV	Patrick Gurian, Nicholas Dudley Ward	R. Weber, J. Proctor	July 24, 25
University of California at Berkeley	Project I	Mark Nicas, Rachael Jones	R. Weber	July 31, Aug 1st
University of Arizona	Project I	Chuck Gerba, Chris Choi, Stephanie Boone, David Greenberg, Jessica Henley, Pedro Romero-Gomez	R. Weber	August 17, 18
Carnegie Mellon University	Project IV	Elizabeth Casman	R. Weber	September 13, 14
Michigan State University	Project I	Syed Hashsham, Amanda, Joan Rose, Tomoyuki Shibata, Yoshifumi Masago, Amanda Herzog	R. Weber	September 26, 27
University of Michigan	Project II	Joe Eisenberg, Jim Koopman, Sheng Li, Ian Spicknall, Josep M Pujol	R. Weber	September 28, 29
Drexel University	Project III	Chuck Haas, Mark Weir, Sushil Tamrakar	R. Weber	October 2

Collaborations outside CAMRA:

Professor Chaomei Chen, from iSchool at Drexel and doctoral student Kaushal Desai. We have been collaborating in investigating the uses of visualization tools for the CAMRA KR.

10. Integration with other projects:

Project V has a unique integration to all other projects because it is responsible for their integration. The connection with all other projects is along the collaboration, sharing, and integration among all projects. There are no technical integrations expected.

11. Tasks for Next Year (see definition below):

Revising Learning Units

Building Version 2.0 of Knowledge Repository

Defining Domain Structure for QMRA

Applying Reasoning Methods on the Knowledge Repository

12. Anticipated Technical Results and Developments (examples of potential learning units for next year, within possible also include potential outcomes):

The revised version of the tool will be robust and fully tailored to the CAMRA community. In one year from now, the tool will be able to issue report draft to guide CAMRA members in writing EPA reports just like this one. The manual work of going over learning units and re-describe them in the report will be automated, leaving more time for scientists to dedicate to their science, and produce more standardized reports that should be easier to be interpreted by EPA.
The domain structure for the domain will be presented based on the contributions to the repository in years I and II and the studies that were carried out in Year I.

References

Szulanski, G. (1996). Exploring Internal Stickiness: Impediments to the Transfer of Best Practice Within the Firm. Strategic Management Journal 17(Special Issue: Knowledge and the Firm): 27–43.

Weber, R., & Aha, D. W. (2003). Intelligent Delivery of Military Lessons Learned. Decision Support Systems, 34(3), 287–304.

Weber, R., Aha, D. W., & Becerra-Fernandez, I. (2001). Intelligent Lessons Learned Systems. *Expert Systems with Applications, 20*(1), 17–3

Table 2: CAMRA Year-1 Expenditure: from September 2005 to August 31 2006

University	Given to Univ.	Project	PI	Given to PI	Expense	(%)
Michigan State University	$ 422,779.00	Co-Director	Dr. Rose	$ 247,282.00	$ 64,294.00	26
		I	Dr. Hashsham	$ 175,497.00	$ 31,415.03	18
		III	Dr. Bolin	$ -	$ -	n/a
		V	Dr. Todd	$ -	$ -	n/a
University of Arizona	$ 203,254.00	I	Dr. Gerba	$ 100,745.00	$ 74,556.00	74
		I	Dr. Choi	$ 102,509.00	$ 80,126.78	78
Northern Arizona University	$ 101,439.00	I	Dr. Keim	$ 101,439.00	$ 13,547.00	13
University of California, Berkeley	$ 157,613.00	I	Dr. Nicas	$ 157,613.00	$ 55,247.86	35
University of Michigan	$ 299,453.00	II	Drs. Eisenberg and Koopman	$ 299,453.00	$ 172,710.00	58
Drexel University	$ 454,326.00	Co-Director	Dr. Haas	$ 106,560.00	$ 26,077.45	
		III	Dr. Haas	$ 107,766.00	$ 30,292.50	28
		IV	Dr. Gurian	$ 90,003.00	$ 23,673.07	26
		V	Dr. Weber	$ 150,000.00	$ 97,434.80	65
Carnegie Mellon University	$ 99,769.00	IV	Dr. Casman	$ 99,769.00	$ 11,739.00	12
Direct Total	$ 1,738,633.00	--	--	$1,738,636.00	$ 681,113.49	39
Indirect Cost	$ 286,367.00					
Total Cost	$ 2,025,000.00					

Note: Official work for all contracts and requirements were completed between April to June 2006 although the CAMRA was established in September 2005. Michigan State University hired one post-doctoral scientist in July and one administrative assistant in October.