



**Center for Advancing Microbial Risk Assessment
Year 5 Annual Report**

Submitted to

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EPA Agreement: RD832262

Investigators: Directors Dr. Joan B. Rose¹ and Dr. Charles N. Haas³; Dr. Carole Bolin¹ and Dr. Syed Hashsham¹; Dr. Elizabeth Casman²; Dr. Patrick Gurian³ and Dr. Rosina Weber³; Dr. Paul Keim⁴ and Dr. David Wagner⁴; Dr. Mark Nicas⁵; Dr. Charles Gerba⁶ and Dr. Chris Choi⁶; Dr. Joe Eisenberg⁷ and Dr. Jim Koopman⁷

Institutions: ¹Michigan State University (lead), ²Carnegie Mellon University, ³Drexel University, ⁴Northern Arizona University, ⁵University of Arizona, ⁶University of California at Berkeley, ⁷University of Michigan

Introduction:

Over the past five years CAMRA (The Center for Advancing Microbial Risk Assessment) has addressed important research questions aimed at understanding the risk of pathogen transport, public exposure and disease transmission in the natural and built environments. Focusing both on natural events and bioterrorism CAMRA had been designing and evolving a new microbial risk framework that advances integration of microbiology, mathematics, engineering, epidemiology and decision making. The five project teams (associated with Project I: Exposure; Project II: Infectious disease transmission; Project III: Dose-response; Project IV: Assessment and analysis, and Project V: Knowledge management and transfer) have completed and published a total of 47 Journal articles (see carma.msu.edu for full list of citations), 8 proceedings papers, 91 conference presentations, trained and graduated more than 20 students, taught five CAMRA Summer Institutes and organized four CAMRA All PI Meetings. The linkages established between projects and universities have resulted in significant development of the QMRA field of science and will now be the basis of the Microbial Risk Wiki to be completed with key data and models accessible for a broad array of pathogens, exposure pathways and venues.

Some of the broad accomplishments for CAMRA investigators at the Center level have been the coalescence around three main pathogens important to bio-terrorism and national health risks as a primary integration of the risk assessment and management framework: *Bacillus anthracis* (*B. anthracis*); *Fransicella tularensis* (*F. tularensis*); and influenza (Figure 1).

B. anthracis was one of the first and main linkages between projects. Project IV required information, data and models to develop characterized risk assessments including dose-response, survival and transference. This led towards development of decision models as a means of informing optimal choices after a release of spores. These assessments were performed in the event of a malicious release, however, the framework can now be expanded to other scenarios and pathogens as well.

Another key pathogen, *F. tularensis*, another category A agent has also been targeted. This pathogen has allowed for crossover from Project III with Project II to develop a series of novel and interesting animal model experiments. Dr. Bolin's laboratory using a true and real oral ingestion route (mice willingly drinking the dosed water) has devised and will begin experiments on multiple dosing and time dependent dosing. These experiments and the design involved the modelers from both Project II and Project III. Project I has focused on gathering information which can be used to define survival of pathogen in the environment.

Influenza was also a main source of collaboration bringing projects together. Experiments performed with the vaccine strain from Project I have developed a great amount of very useful data on the role of hands and fomites. Project II worked with Project III to determine the best dose response models and construct the overall tool taking in account the various transmission routes for influenza (also informed by Project I). An overall decision support tool was designed and constructed by Project IV. This tool accounts for the effectiveness and costs of different risk mitigation strategies (informed by Project IV). This overall tool has the potential for widespread use and has already been tested for use at the (QMRA) Summer Institute where students evaluated its ease of use and effectiveness in scenario evaluation.

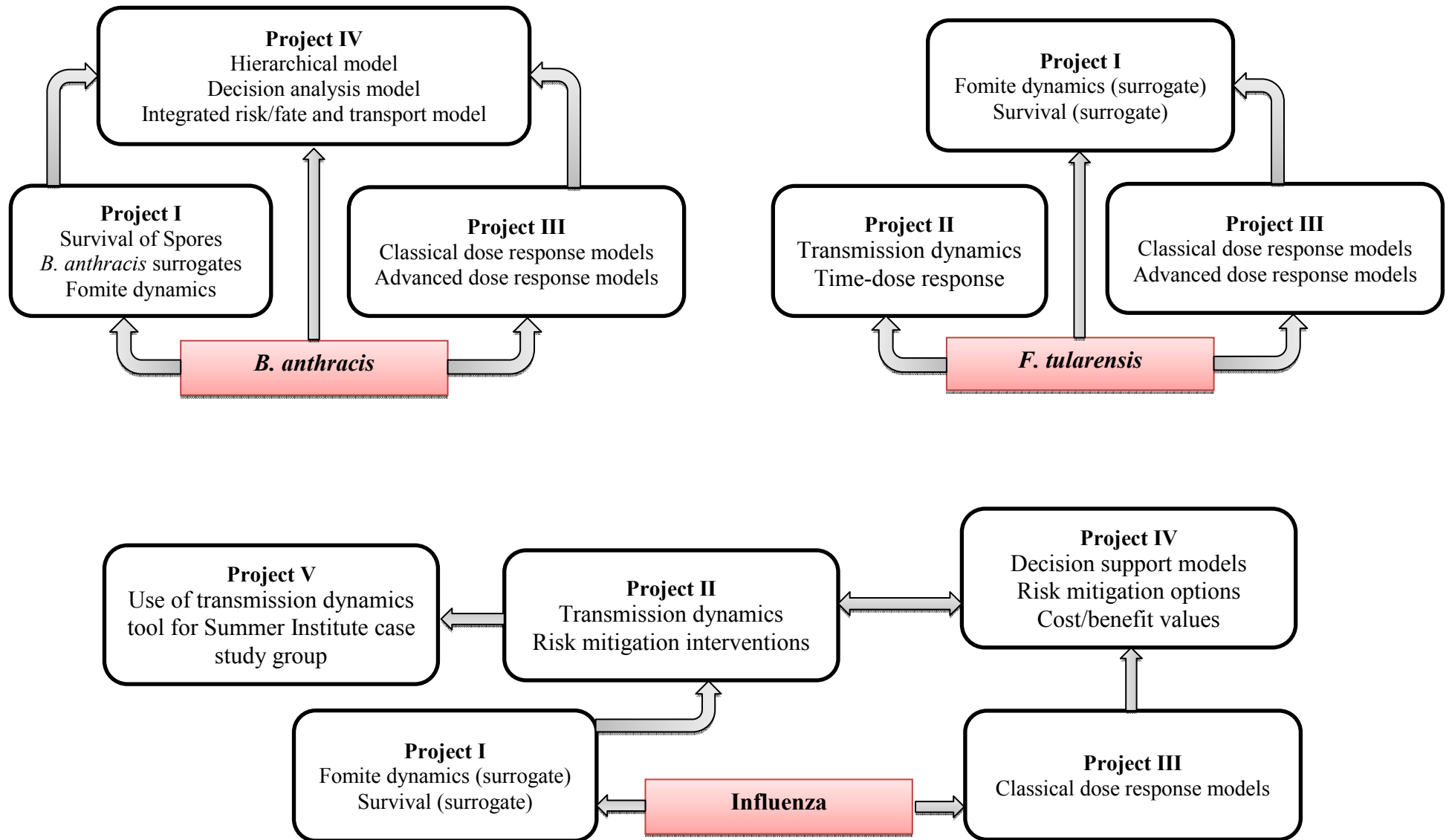


Figure 1. CAMRA development of tools, methods and models focusing on Anthrax , Influenza, and Tularemia

Summary of Key Findings and Accomplishments:

Overall in 2010, CAMRA has produced 11 peer reviewed publications and investigators and students have made 16 presentations. Two QMRA workshops were completed and the 5th QMRA summer institute was taught. CAMRA continues to produce high quality QMRA students

Table 1 Key accomplishments 2010.

Accomplishment Type	Amount
Peer reviewed publications	12
QMRA Newsletters	3
Master's theses	1
Doctoral theses	3
Participation at DHS; NBACC workshops	2
Conference presentations	16
Workshops	<p>5th QMRA Summer Institute</p> <ul style="list-style-type: none"> • Hosted by Dr. Gertjan Medema, TU Delft, The Netherlands • 29 Students (10 government, 2 private company, 17 academic) • 16 Countries (Australia, Czech Republic, Belgium, Germany, Switzerland, Ghana, Finland, Sweden, The Netherlands, Denmark, Latvia, Spain, Singapore, Saudi Arabia and Uganda) <p>International Water Association World Water Congress</p> <ul style="list-style-type: none"> • Instructors: Dr. Charles N. Haas, Dr. Gertjan Medema, Dr. Joan B. Rose and Dr. Mark H. Weir • 45 Congress Delegates in attendance • Showcased some key outputs from CAMRA
Sponsored students	15
Students graduated	4
Visiting Scholars and Post-doctoral scientist	10
Year 5 Things In Progress Learning Units	19
Year 5 Things I Have Completed Learning Units	19
Year 5 Learning units showing associations	22

CAMRA Project I has published a complete review and analysis of detection limits for rapid molecular techniques for *B. anthracis*. This work presents the limitations of a complete QMRA for the indoor environment addressing the underlying uncertainty. Project I has also been in collaboration with Project II to produce and publish recommendations for limiting routes of exposure for influenza. Along with these key accomplishments Project I has also contributed to water systems security by advancement of their vital work on the comprehensive solute mixing model, AZRED for microbials. AZRED II which will soon be widely available has furthered the accuracy of EPANET as it incorporates axial dispersion as well as junction issues for water distribution systems.

Project II has worked closely with Project I to develop risk based intervention strategies to mitigate influenza exposure. Project II has also made significant progress towards dose timing models. This model takes into account some of the preliminary data from Dr. Carol Bolin's animal model data, as

well as previous modeling work, to develop a dynamic risk model using exposure patterns for *B. anthracis*.

Project III has continued the reporting on dose response models increasing the growing catalogue of dose-response parameters for all Category A and B organisms. The Rickettsia group has now been modeled as well as *Brucella* (causative agent of brucellosis). One of the main advancements made is the progress on developing a mechanistic dose response model which is capable of incorporating immunity as a factor for *B. anthracis*.

Project IV has teamed with Projects I and III to develop a model which links environmental concentration and risk from exposure to a series of pathogens. The framework has been established based on Norovirus, *Variola major* (*V. major*) and *F. tularensis*. Integrating dose response models from Project III and persistence data from Project I these models can quantify the prioritization of future research to different agents.

Project V has continued work towards improving the knowledge repository and making the system as user friendly as possible. There has also been a large amount of work to develop a microbial risk wiki. The wiki will be a publicly available warehouse of information data and models (see below).

Project V has also hosted a number of visiting scholars and researchers. These scholars sought out CAMRA as a central location to learn and gain research experience with QMRA.

Dr. Maria Tereza Peppe Razzolini, came to MSU as a visiting Assistant Professor for the School of Public Health at the University of São Paulo. Maria worked with Drs Rose and Weir on two main projects to learn applied QMRA techniques and mathematical modeling. First Dr. Razzolini brought data on *Giardia* concentrations from shallow wells in peri urban areas around the São Paulo region, with the goal of modeling the risk to users of this water. This work was completed and a publication has been accepted by the *International Journal of Environmental Health Research*. The second project Dr. Razzolini worked on was a risk assessment to inform engineering design recommendations for a recreational spray park which experienced a *Cryptosporidium* outbreak. This second project is currently under review for publication in *Water Research*.

Dr. Stephanie Luster-Teasley is an Assistant Professor at North Carolina Agriculture and Technology (NCA&T). Dr. Luster-Teasley came to MSU to work with Drs Rose and Weir as part of the Minority Serving Institution (MSI) research program through Department of Homeland Security. Two Masters level students Mr. Christopher Jackson and Ms Chanel Rogers were also funded to continue their research experience as mentees of Dr. Luster-Teasley on an advanced oxidant that she has been developing. Dr. Luster-Teasley and her students examined inactivation of bacteria and viruses and developed a QMRA based on these results. Dr. Luster-Teasley applied for follow up funding to continue her experimental and risk work with Dr. Weir through DHS as part of the MSI research program. This work will generate 2 or more publications in year 6.

Project V also hosted two visiting student scholars over the summer of 2010. Ms. Johanna Marcela Soto Beltran a PhD candidate at the University of Arizona visited MSU to learn QMRA and start her QMRA research portfolio. Ms Soto assisted with the modeling of the inactivation kinetics of Dr. Luster-Teasley's disinfectant as well as the QMRA modeling. Mr. Mohammed Firdaus Hamzah, visited MSU from the Nanyang Technological University, Singapore. Mr. Hamzah explored development of a transmission model of *cholera* in a small village in the developing world.

Advances in QMRA is the quarterly newsletter (issues were released in January, April, July, and October) compiled by CAMRA staff. This four page newsletter aims to keep CAMRA staff, students and members a breadth of the ongoing research by highlighting projects at all partnering Universities and providing one of several outlets for informing the CAMRA community of pertinent news items, including upcoming workshops. The newsletter is distributed via email to 133 CAMRA listserv subscribers and is also posted on the CAMRA website at <http://camra.msu.edu/news.html>.

Finally progress has been made toward the QMRA wiki. CAMRA determined that a wiki would be an ideal option for disseminating the large amount of CAMRA information and data to the microbial risk assessment community of scientists. The wiki will be a great option for developing a

greater community of QMRA researchers and users since it is being built as an instructional tool as well. Currently the Wiki is being populated with dose response data (Figure 3 is a screenshot of a dose response dataset available). The wiki will be further developed to contain specific models developed for pathogens, inactivation parameters and various exposure routes as well as venues which have been evaluated by CAMRA. This will be designed so others can begin to contribute to the data base and information in the WIKI.

In support of the wiki CAMRA is currently writing a dose response monograph. This monograph is being prepared for review and release in year 6 and is envisioned to be a central reference for those researchers and scientists interested in QMRA and dose response modeling. The monograph will include a brief description of the derivation of dose response models and the mechanics of optimizing the models from both animal and human data sets. The subsequent chapters will present the optimized dose response models for specific pathogens which animal or human data was gathered by CAMRA or the researchers' prior work. The monograph will be linked integrally with the wiki so that the data sets described in the monograph will be available in the dose response section of the wiki for user's own use of the data.

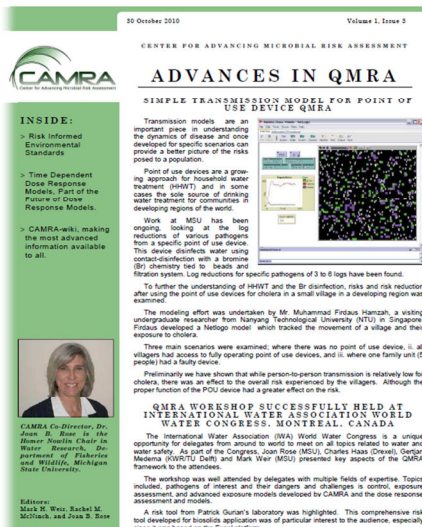


Figure 2. Cover page of CAMRA QMRA newsletter

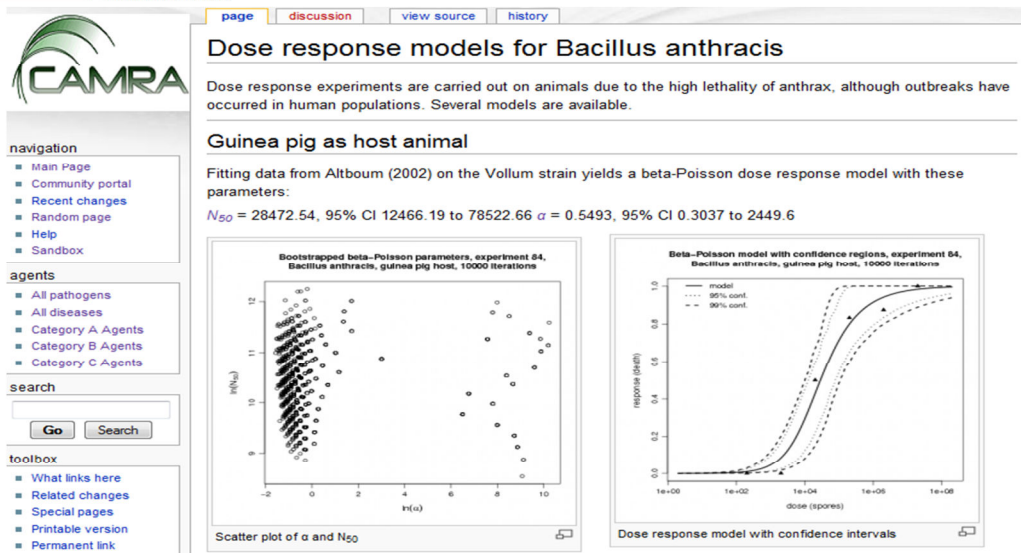


Figure 3. Screenshot of CAMRA QMRA wiki

Project Specific Reports:

Project I: Exposure: Detection, Fate and Transport of Biological Agents of Concern (BAC)(Gerba, Nicas, and Choi).

There are a number of key gaps in advancing and understanding the full picture of microbial risk assessment. One is a better understanding of the interaction between humans and fomites especially in the indoor environment. This key gap with fomites is in understanding the transfer efficiency from fomites to hands. Exposure from potable water supplies has moved forward as well, where additional complicating factors have been included into the advances made to EPANET already developed by Project I. In addition to the continued work in potable water exposure modeling, the integration of risk estimation is being included as well, so that exposure and risk estimation will be innately combined. Along with water and fomite exposures, a greater understanding and quantification of the droplet spray dynamics has been completed.

One of the key needs for advancing microbial risk assessment is an understanding of the interaction between person and fomite (Gerba). For this gap data on the transfer efficiency of microorganisms from fomites to hands is required. The transfer efficiency of *Escherichia coli*, coliphage MS-2, and *Bacillus thuringiensis* spores was assessed using various fomite surfaces (i.e. Acrylic, stainless steel, Formica, glass, ceramic tile, cotton, polyester and paper money). These were assessed under two different relative humidity conditions (i.e. 20 to 30% and 45 to 65%). The transfer efficiency varied greatly among the different fomites (Figure 2) with hard surfaces such as stainless steel Formica and acrylic plastics having the greatest efficiency of transfer, with fabrics and paper having the lowest. The differences in transfer efficiency among the different organisms were not large, but virus transfer was somewhat greater than the other organisms. Although all of the data have not been analyzed to date greater transfer appeared to occur at the higher relative humidity. The data are currently being analyzed to determine if statistical differences exist between the studied parameters.

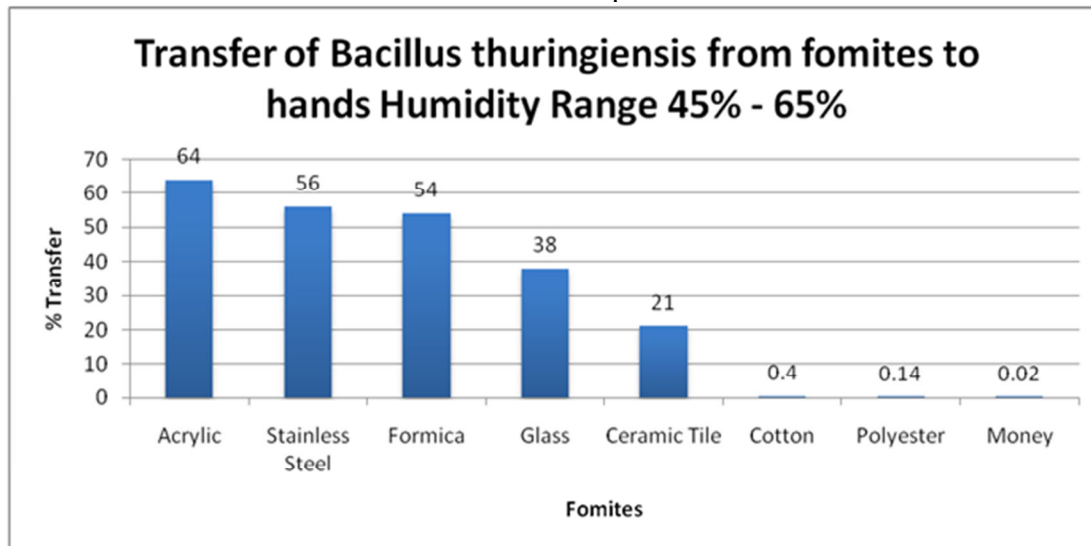


Figure 2. Transfers from fomites to hands for a number of common fomites under differing environmental conditions.

A second means of exposure assessment is addressing droplet spray which refers to respiratory fluid particles that upon emission during coughing, sneezing or speaking by one person, ballistically striking the eyes, nostrils and lips of a second person (Nicas). Such exposure

requires “close contact” because the relatively large particles involved do not travel far in air before falling out due to gravity. Most infection control professionals and infectious disease epidemiologists believe that droplet spray exposure is an important transmission pathway for respiratory disease pathogens such as influenza virus, SARS corona virus, and pneumonic plague.

Water quality models of potable water distribution systems are improved by including transport phenomena which accurately represent mixing at junctions (as well as previous work of including axial dispersion) (Choi). Including these phenomena helps to represent the solute transport within potable water networks. Previous computational and experimental studies have supported the assumption that mixing at junctions is incomplete rather than complete, as has been conventionally assumed. In addition, a recent study proposed, and experimentally verified, that dispersion coefficients could be used effectively in pipelines under laminar flows. This ongoing work incorporates incomplete mixing at junctions with the already established axial dispersion work from year-4 (AZRED). First, hydraulic calculations in a selected network will provide the database for water quality simulations that involve incomplete mixing at junctions. Next, a 1D dispersion-advection model, integrated with recently developed coefficients, will produce transient water quality results for the network. The results will be quantitatively compared with those obtained based on the conventional assumptions (i.e. complete mixing and advection-only solute transport). Finally, axial dispersion will be embedded into the AZRED code in order to fully integrate both of the improved transport assumptions for water quality analyses. The broad goal of this research is to emphasize the importance of the water quality modeling that utilities use to obtain the predictions they need in order to make pressing decisions, such as those pertaining to operation, microbial risk assessment, and the early warning systems designed to detect contamination events.

The process of incorporating a risk estimation subroutine with the advanced AZRED model has been initiated. This work is intended as an event based risk estimation approach, in order to assess the risks from high impact contamination events. *Cryptosporidium* is being used as the model pathogen, but results are also intended to give general information about the characteristics of contamination events in water distribution networks. Uncertainty in the risk assessment is being modeled using the Monte Carlo method as a subroutine within EPANET (including the AZRED adaptation) to simulate the hydraulics and water quality. An example network is used to simulate contamination events. The response action considered is a stop use order triggered by a network of sensors in the distribution system. This model will help with a better understanding of sensor location as well as demonstrate the usefulness of sensors in a potable water distribution system.

Project II: Infectious Disease Models for Assessing Microbial Risks for Developing Control Strategies (Eisenberg and Koopman)

A means of advancing microbial risk assessment is garnering an understanding of the role of the environment in disease transmission. Project II has been working towards comprehensive environmental infection transmission systems (EITS). This comprehensive modeling framework has been developed in past years, and is now being refined. Tools have been developed for model identification and choice of what model to use. Project II team members have examined biological and environmental contexts to determine the dominant modes of influenza transmission. This analysis helps to inform decision makers on the optimal intervention options

for the current H1N1 pandemic. This work has been extended in two ways. First, in examining how surface touching patterns alter hand hygiene and surface decontamination efficacy. Second, how the efficacy of these two environmental interventions vary across 3 distinct pathogens: Influenza, norovirus, and MSRA.

Other work has progressed on a dynamic dose response model taking into account exposure patterns in risk assessment. A case study was developed for inhalational anthrax which provided: 1) an approach to assessing the risks associated with exposures that vary over time; 2) evidence that dose timing and dose order matters with respect to risk estimates; and 3) a tool for helping to design further multiple dosing studies that can further inform us on the importance of dose timing and order and provide data to help refine our dynamic dose response models. This work contributes to a more realistic model of fomite mediated transmission.

Understanding transmission after an outbreak event is a limiting factor in heavily transmissible diseases such as norovirus. A case study was developed to utilize an EITS framework and statistical analysis of household norovirus transmission from point sources after an outbreak in the household. This work progresses towards further broadening the EITS framework to include developed cumulative dose response models.

Project III: Dose Response Modeling and Application (Haas and Bolin)

Modeled dose response relationships are a critical step in quantifying a risk estimate. Project III has continued to catalogue animal model and when applicable human dose response data for use in model optimization. These modeled dose response relationships can be used to address how the risk of an adverse event varies with the dose of the selected pathogen. These relationships modeled are now being used to advance the QMRA in specific scenarios:

- The release of *Cryptosporidium* through a water distribution system (exposure modeling led by Project I) and the associated risks.
- The indoor release of *B. anthracis* including fate and transport through the indoor environment, and the associated risks to the population.
- Post remediation residual concentration of pathogen(s) posing a residual risk to the population using the contaminated space again. Linking with Project IV to assess the appropriate remediation level for the scenario considered.

Also during this year, updated dose response models for *Rickettsia rickettsia*, *Rickettsia typhi* and *Brucella suis*, *Brucella melitensis* (*Br. melitensis*) and *Brucella abortus* were developed. Also investigate was the effect of aerosol particle diameter on the dose response for *Francisella tularensis* (*F. tularensis*). A pooled animal-human time post inoculation (TPI) dose response model was used to analyze two laboratory outbreaks of *Br. melitensis* and estimate initial exposure doses to the patients. The development of models incorporating time to effect (i.e. what the time distribution of cases following an exposure) have provided essential insight into analysis of a number of outbreaks for several microbial diseases. These TPI modeled diseases include *Yersinia pestis*, *F. tularensis*, *Mycobacterium tuberculosis* and *B. anthracis*. This study has resulted in a successfully defended doctoral dissertation.

The project III team at Drexel has been working with the project III team at Michigan State University (MSU) to obtain new experimental data on the response of animals to oral ingestion of *F. tularensis* that will be used for the development of improved TPI based dose response models. By comparison of the data obtained in these explicitly designed experiments with the data from the literature on inhalation dose response, extrapolation of risks between different portals of entry can be performed.

The MSU research team of Project III has been incapable of performing tasks for year 5 due to serious illness of the PI (not related to work with CAMRA). No year 5 funds were used by the PI during this time. The work on animal model experiments will continue in the first quarter of 2011. These tests will continue the multiple dosing scheme devised with the input from Project II and Drexel Project III.

Project IV: Assessment-Analysis Interface (Gurian and Casman)

Project IV has been concerned with a number of different scenarios which cross cut topics and projects throughout CAMRA. One of these is the air deposition model that was developed in previous reporting years. This model has been validated with data obtained from both the Idaho National Laboratories (INL) study and the Hart Senate Office Building (HSOB). As the National Institutes of Standards and Technology (NIST) is considering validating a completely mixed flow model to the INL data and that the HSOB data involved actual *B. anthracis* spores under more realistic conditions, this data source was chosen for model validation. While the HSOB data is most suitable to indoor air transport modeling the INL data is best suited to analysis of recovery efficiencies of different surfaces under field conditions. This analysis of surface recovery efficiencies is currently underway and will continue into the next funding year.

Project IV has also conducted the survey on influenza risk perception and decision making. This survey captured the responses of 188 adult participants, who were primary caretakers of children under the age of 10. The results of this survey are currently under analysis. Survey work has also been commenced with the Rand Corporation's American Life Panel including a national sample of 2,694 participants in a longitudinal internet panel study. These survey results are currently undergoing analysis and will continue into next year.

Project V: Knowledge Management Learning and Discovery (Weber, Weir and Rose)

Project V at Drexel University has been analyzing the interaction of CAMRA researchers and modeling the interactions made. Models of the interactions of multidisciplinary collaborators in an academic context is an interesting addition to the literature. Project V at Drexel has also been adapting the Knowledge Repository (KR) to the needs of CAMRA as well as maintaining the KR itself.

Project V at MSU has been developing and preparing data for inclusion into the microbial dose response wiki. The wiki is intended as a learning tool for the public interested in learning about QMRA as well as a readily available location for sharing work developed by CAMRA.

The annual CAMRA summer institute this year was hosted by one of our science advisory committee members. Dr. Gertjan Medema of Delft Institute of Technology in the Netherlands led the organization and execution of the summer institute. This was an exciting opportunity to expand the reach of knowledge of QMRA to other partner nations. Among the 29 students in attendance 16 countries were represented (Australia, Czech Republic, Belgium, Germany, Turkey, Switzerland, Ghana, Finland, Sweden, The Netherlands, Denmark, Latvia, Spain, Singapore, Saudi Arabia and Uganda). The mix of disciplines ranged from an undergraduate engineering student, to microbiologists and other scientists holding PhDs, and health officials. As in the past, the case study portion of the program was likely the best means of students learning the science and execution of QMRA. Topics for this summer institute included;

1. Q-fever in smallholder farms and associated risks of airborne exposure to the public

2. Potential inhalational Legionella exposure from tap water used as a replacement for windshield washer fluid
3. QMRA based evaluation and recommendations for sustainable urban storm water systems used as recreational sites
4. Use of reclaimed wastewater for irrigation water supplies and the associated risks to consumers and farmers
5. Recommendations for consumer protection from a brief water treatment plant lapse in operation

The students generated full reports containing their entire analyses as well as recommendations that were possible given the data and information available. The students also presented their results to their peers at the end of the week.

Based on this summer institute in The Netherlands the framework and layout of the program has proven its ability to be exported and used in different settings. Also not all of the typical instructors were available to lecture at this institute. Dr. Joan B. Rose, Dr. Charles N. Haas, Dr. Mark H. Weir, and Dr. Gertjan Medema, were the only instructors at the 2010 institute who have lectured in past institutes. The new instructors (listed below) adapted quickly to the fast pace and intensive learning environment. This was a good result showing that the format can be expanded and developed for other groups and audiences.

1. Dr. Arno Swart, National Institute of Public Health and the Environment, The Netherlands (RIVM)
2. Dr. Helene Voeten, GGD, Rotterdam-Rijnmond Public Health Service, The Netherlands
3. Dr. Fred Woudenberg, GGD Amsterdam Public Health Service, The Netherlands
4. Dr. Peter Teunis, RIVM, The Netherlands
5. Dr. Ana Maria de Roda Husman, RIVM, The Netherlands
6. Dr. Patrick Smeets, KWR Watercycle Research Institute, The Netherlands

Appendix A: Summary of Accomplishments

Publications

(Peer reviewed journals)

Greenberg, D. L., J. D. Busch, D. M. Wagner and P. Keim (2010). "Identifying experimental surrogates for *Bacillus anthracis* spores: a review." *Investigative Genetics* 1(4).

Gunawardena, S., R. Weber and D. E. Agosto (2010). "Finding that Special Someone: Modeling Collaboration in an Academic Context." *Journal of Education for Library and Information Science* 51(4).

Hong, T., P. L. Gurian and N. Ward (2010). "Setting Risk-Informed Environmental Standards for *Bacillus Anthracis* Spores." *Risk Analysis* 30(10): 1602-1622.

Huang, Y. and C. N. Haas (in press). "Quantification of the relationship between bacterial kinetics and host response for monkeys exposed to aerosolized *Francisella tularensis*." *Applied and Environmental Microbiology*.

Huang, Y., T. Hong, T. A. Bartrand, P. L. Gurian, C. N. Haas, R. Liu and S. B. Tamrakar (2010). "How Sensitive Is Safe? Risk-Based Targets for Ambient Monitoring of Pathogens." *IEEE Sensors Journal* 10(3): 668-673.

Mayer, B. T., J. S. Koopman, E. L. Ionides, J. Pujol and J. N. S. Eisenberg (in press). "A dynamic dose-response model to account for exposure patterns in risk assessment: a case study in inhalation anthrax." *Journal of the Royal Society Interface*.

Mitchell-Blackwood, J., P. L. Gurian and C. O'Donnell (in press). "Finding Risk-based Switchover Points for Response Decisions for Environmental Exposure to *Bacillus anthracis*" submitted to *Human and Ecological Risk Assessment*.

Razzolini, M.T.P., Weir, M.H. Matte, M.H., Matte, G.R., Fernandes, L.N. Rose, J.B. (accepted) Risk of *Giardia* infection for drinking water and bathing in a peri-urban area in São Paulo, Brazil. *International Journal of Environmental Health Research*

Romero-Gomez, P., K. E. Lansey and C. Y. Choi (in press). "Impact of an incomplete solute mixing model on sensor network design." *Hydroinformatics*.

Spicknall, I., J. Koopman, M. Nicas, J. Pujol, L. Sheng and J. Eisenberg (2010). "Informing Optimal Environmental Influenza Interventions: How the Host, Agent, and Environment Alter Dominant Routes of Transmission." *PLoS Computational Biology* 6(10).

Tamrakar, S. B., A. Haluska, C. N. Haas and T. A. Bartrand (in press). "Dose-Response Model of *Coxiella burnetii* (Q Fever)." *Risk Analysis*.

Zelner, J., A. A. King, C. L. Moe and J. N. S. Eisenberg (2010). "How Infections Propagate After Point Source Outbreaks: An Analysis of Secondary Norovirus Transmission." *Epidemiology* 21(5): 711-718.

(Peer Reviewed Proceedings)

none

(Book Chapters)

none

(Theses / Dissertations)

1. Pedro Romero-Gomez, University of Arizona, 2010. Doctoral Dissertation. Transport phenomena in drinking water systems. Supervised by Professor Christopher Choi.
2. Jade Mitchell-Blackwood, Drexel University, 2010. Using Analytic Models to Address Uncertainty and Establish Thresholds for Risk-Based Responses to Pathogenic Agents in the Environment. Doctoral Dissertation. Supervised by Professor Patrick Gurian.
3. Yin Huang, Drexel University, 2010. Doctoral Dissertation. Incorporating Time to Response into Dose-Response Models Used in Quantitative Microbial Risk Assessment. Supervised by Professor Charles Haas.
4. Ian Solon, Drexel University, 2010. Master Thesis. The extraction of a *B. anthracis* Surrogate from Pleated HVAC Filters. Supervised by Professor Patrick Gurian.

(Un-refereed documents)

none

Presentations**(Conference)**

- Austin, R. G., C. Y. Choi, P. L. Gurian, T. C. Balagopal, Event-Based Microbial Risk Assessment and Response Analysis of Cryptosporidium in Municipal Water Distribution Networks, Water Distribution Systems Analysis (WDSA), Tucson, AZ, September 12-15, 2010.
- Andrade, M. A., F. Rojano, P. Romero-Gomez, and C. Y. Choi, Integrated Water Quality Modeling of Water Distribution Systems, Water Distribution Systems Analysis (WDSA), Tucson, AZ, September 12-15, 2010.
- Bruine de Bruin, W., Parker, A.M., & Maurer, J. Measuring perceived invulnerability to H1N1 (swine) flu risks. Invited presentation at the Workshop on Internet Interviewing about Health and Retirement, Munich Germany, March 22, 2010.
- Gunawardena, S., Weber, R., & Agosto, D. E. Finding that Special Someone: Modeling Collaboration in an Academic Context. Presented at Creating a Culture of Collaboration, 2010 ALISE Annual Conference, Boston MA, January 12-15, 2010.
- Gurian, P., Tao Hong, Jade Mitchell-Blackwood, Ian Solon, Charles Haas, Nicholas Dudley Ward, Yin Huang, Cara O'Donnell, Hernando Perez, "Responding to Bioterrorism: From Risk Assessment to Risk Management" Fourth Annual University Network Summit, Washington, DC, March 10, 2010.
- Herzog, Amanda B., Alok K. Pandey, Prianca Bhaduri, Charles P. Gerba, Joan B. Rose, and Syed A. Hashsham. Evaluation of Recovery Efficiency and Survival of Bacteriophage P22 and *Bacillus thuringiensis* on Fomites". Michigan Branch of the American Society for Microbiology Fall meeting "Microbiology Method for Education and Exploration" on October 8-9, 2010.

Hong T, Gurian P, Identifiability of Bioaerosol Transport and Risk Models by Environmental Sampling, presented at the Society for Risk Analysis Annual Meeting, Baltimore, MD, December 6-9, 2009.

Huang, Y. and Haas, C.N. Time-dose-response Model. Poster presented at the Society for Risk Analysis Annual Meeting, Baltimore, MD, December 6-9, 2009. Winner of the Dose-Response Student Merit Award, Biological-Stressors Student Merit Award, and the Best Poster Award.

Huang, Y and Haas, C.N. How Clean Is Clean? Risk Assessment for *Francisella tularensis* in Water. PA Section AWWA 2010 Conference, Lancaster, PA, May 11 to 13, 2010.

Romero-Gomez, P., D. Kang, G. Wood, C. Y. Choi, A Game Theory Approach for De-centralization of Reclaimed Water Systems, Water Distribution Systems Analysis (WDSA), Tucson, AZ, September 12-15, 2010.

Spicknall, I.H. Eisenberg, J.N.S. Dominant Modes of Influenza Transmission: An Epidemiologic Perspective. Joint Conference of International Society of Exposure Science International Society for Environmental Epidemiology, Seoul South Korea, 2010.

Madsen, J.M. and P.L. Gurian "Valuing Environmental Detection of a B. anthracis Release," Society for Risk Analysis Annual Meeting, Baltimore, MD, December, 2009.

Mayer B. Presentation to the Environmental Protection Agency, Homeland Security, and CAMRA regarding work on time-dependent dose-response modeling results on anthrax infection in monkeys, Cincinnati, 2009.

Mitchell-Blackwood, J., P.L. Gurian, and the Physiological Assessment of Microbial Effects (PhAME) Workgroup: B. Thran, S. Taft, R. Lee, and S. Hines, "Development of Dose-Response Curves for *Bacillus anthracis* Using a Bayesian Approach on Historic Data," Annual Meeting of the Society for Risk Analysis, Baltimore, MD, December 2009. SRA Biological Stressors Specialty Group (BSSG) Student Merit Award.

Mitchell-Blackwood J. and P.L. Gurian, "Developing Predictive Models for Addressing Uncertainty in Dose-Response of Pathogenic Agents," National Science Foundation (NSF) Graduate STEM Fellows in K-12 Education Annual Conference, at the National Science Foundation, Arlington, VA, March 2010.

Ryan, M., P. Duzinski, P.L. Gurian, C.N. Haas, J.B. Rose. "Acceptable Microbial Risk: Benefit-Cost Analysis of a Boil Water Order for *Cryptosporidium*" Society for Risk Analysis Annual Meeting, Baltimore, MD, December, 2009.

Workshops

International Water Association World Water Congress.

19 September 2010. Montreal, Quebec, Canada

- Dr. Joan B. Rose – Introduction and Background of QMRA
- Dr. Gertjan Medema – Knowing Your Enemy, Pathogens of Concern
- Dr. Charles N. Haas – Dose Response Assessment, Modeling Risk
- Dr. Mark H. Weir – Exposure Assessment and Advanced Exposure Models
- Dr. Mark H. Weir – Wrap up and Discussion

5th Annual QMRA Summer Institute.

19-25 June 2010. TU Delft. Delft, The Netherlands

- Dr. Gertjan Medema – Introduction to QMRA
- Dr. Joan B. Rose – Waterborne Pathogens
- Dr. Arno Swart – Airborne Pathogens
- Dr. Mark H. Weir – Statistics and Uncertainty
- Dr. Mark H. Weir – Monte Carlo Modeling and Working with Crystal Ball
- Dr. Gertjan Medema – Design of QMRA
- Dr. Joan B. Rose – Exposure Assessment Methods for Detection of Microorganisms
- Dr. Arno Swart – Fate and Transport Models – Air
- Dr. Helene Voeten – Risk Perception
- Dr. Fred Woudenberg – Risk Communication
- Dr. Charles N. Haas – Animal and Human Studies & Dose Response Models
- Dr. Peter Teunis – Dealing with Heterogeneity
- Dr. Gertjan Medema – Risk Characterization
- Dr. Ana Maria de Roda Husman – Application of QMRA for Viruses in the Environment
- Dr. Patrick Smeets – QMRA-Based Risk Management

Appendix B: Knowledge Repository Summary Reports

Project I Report by Charles P. Gerba

CAMRA Report for Year V (15 Sept 2009 to 14 Sept 2010) for Project I

1. Project I
2. Investigators: Christopher Choi, Mark Nicas, David Wagner, Scott McLennan , Ian Pepper, Paul Keim, Syed Hashsham, Ryan Sinclair, Sonia Fankem, Pedro Romero, Ryan Austin, Amanda Herzog, Inhong Song, Jessica Henley, Alok Pandey, William McGarry, Andrew Lerch, Charles Gerba, Joan Rose, Kyle Enger, Dawn Birdsell
3. Project Goals:
4. Tasks for Year V (15 Sept 2009 to 14 Sept 2010):

Dr. Charles P. Gerba's Laboratory (University of Arizona)

- 1.) Complete collection of data on the transfer and survival of non-pathogenic surrogates (MS-2 coliphage, *Escherichia coli*, a gram positive bacterium, *Bacillus* spp. spores). Will be used to assess the transfer from contaminated hands to fomites and from contaminated fomites to hands.
- 2.) Since bacteria which possess a lipid membrane may have different transfer rates survival and transfer experiments will also be conducted with vaccine influenza virus.
- 3.) Data gathered in objectives 1 and 2 will be analyzed relative to the various study factors and placed in a spread sheet to be usable by groups II and IV in risk model assessment.
- 4.) Assessment of human collagen artificial skin for use in transfer experiments involving bio-threat agents.

Dr. Christopher Choi's Laboratory (University of Arizona)

- 1.) Effects of the axial dispersion coefficients in water distribution systems and updated AZRED (improved adaptation of EPANET)
- 2.) Event based microbial risk assessment and response analysis of *Cryptosporidium* in potable water distribution systems

Dr. Mark Nicas' Laboratory (University of California Berkeley)

- 1.) Influenza RNA viruses in hospitals during the 2010/2011 winter flu season at Moffitt Hospital. Testing with qPCR of; air, surfaces and protective equipment of nurses attending Influenza A and B patients.
- 2.) Human study in 2010/2011 winter flu season to provide direct estimate of number of viruses to be delivered to facial target sites via droplet spray pathway.

5. Research Activities

Researcher Name	Research Activity
Christopher Choi	Experimental and modeling data comparison and analyses Evaluation of cryptosporidium contamination events and corresponding risk assessment
Ryan Austin	Development of contamination scenarios and risk assessment
Pedro Romero	Theoretical approaches and computational modeling Run Computational Fluid Dynamics and accumulate data sets to support the theoretical foundation
Alex Andrade	Experimental verification and AZRED coding
Amanda Herzog	Evaluating detection limit Investigating detection limit Analyzing data Analyzing Availability of DNA
Charles Gerba	Conducting exposure assessments
Mark Nicas	Analyzing risk assessment Modeling Transfer Testing models Measuring exposure Modeling fate and transport
David Wagner	Identifying experimental surrogates
Syed Hashsham	Evaluating detection limit

6. Background and prior research:

7. Research Contributions this Year:

1. Monte Carlo QMRA in Drinking Water Systems Things that are in progress LU (863)

Author(s): Ryan Austin

When Creating risk assessment we wanted to both improve exposure assessment through a more detailed simulation model, and to do a sensitivity analysis to determine which parameters are important to this assessment.

Experimental Design was as follows:

The unit is an event based risk assessment using a Monte Carlo simulation of a water distribution system. C++ will be used along with the EPANET toolbox to simulate water contamination events which will be summarized in a text file. The text file will then be through a Matlab program that will determine the population infected via dose response data.

Detection limits of all methods for influenza Things that are in progress LU (909)

Author(s): Amanda Herzog

When Evaluating detection limit we wanted to find out The detection limit for all methods detecting influenza

Experimental Design was as follows:

Literature from published journal articles on the detection methods for the organism of interest will be reviewed. Journal articles will be collected using a number of key words on ISI Web of Science.

References will be exported into an EndNote file. A manual screening will be conducted to eliminate any references that were not expected to contain relevant data.

Evaluation of environmental detection limit *B. anthracis* Things that are in progress LU (910)

Author(s): Amanda Herzog

When Investigating detection limit we wanted to find out The environmental detection limit and parameters which may affect recovery of the sample.

Experimental Design was as follows:

B. thuringiensis will be spiked into soil and water samples with various characteristics. Parameters affecting the recovery and detection will be evaluated.

Experimental Verification of AZRED II Things that are in progress LU (1100)

Author(s): Christopher Choi

When Estimating water quality we wanted to find out We hypothesize that AZRED II can handle both axial dispersion and junction issues to predict accurate water quality in pipe systems.

Experimental Design was as follows:

We intend to validate the newly developed code, AZRED II, in a pilot scale system.

2. Salt tracer transport study in a 5x5 water pipe network (595,918)

Things that are in progress LU 595

Author(s): Inhong Song

and Things that I have completed LU 918

Author(s): Christopher Choi

When Modeling transport we wanted to find out Solute or any agents are to be dispersed as it travels through the water pipe lines. The objective of this study is to quantify or characterize the extent of dispersion and improve the water quality modeling performance by incorporating dispersion factor.

Experimental Design was as follows:

Salt tracer dispersion through a water pipe line will be characterized by correlating dispersion coefficients with corresponding hydraulic condition. The dispersion is investigated experimentally and computationally with CFD modeling. The characterization results of dispersion are to be incorporated into water quality modeling. Then, a transient pulse flow will be introduced into the 5 by 5 network and the spatial as well as temporal salt spread through the network will be monitored. The same experimental setup will be simulated with the dispersion incorporated model and the experimental data will be used to verify the model performance.

Contribution:

Water quality models based on accurate mixing data at cross junctions are important for estimating concentrations of chemical species in municipal water distribution systems.

The present study indicates that the instantaneous complete thus $\bar{u} \frac{1}{2} \tau$ perfect $\bar{u} \frac{1}{2} \tau$ mixing assumption can result in an erroneous prediction of water quality.

Results:

The perfect mixing model consistently overestimated solute dilution at cross junctions and predicted evenly distributed solute concentration throughout the network. In contrast, the incomplete mixing model demonstrated uneven distribution patterns with a distinct solute plume, and the corresponding results were significantly more accurate than those based on the perfect mixing assumption. Average prediction errors in tracer concentrations were 15 and 66% using the updated and perfect mixing models,

respectively, and the difference was statistically significant P-value of 0.001. Therefore, this study concludes that the incomplete mixing model can drastically improve the prediction of solute transport in pressurized pipe systems that have multiple cross junctions.

Evaluation B. thuringiensis recovered from fomites-cultivation (104,1053)

Things that are in progress LU 104

Author(s): Amanda Herzog

and Things that I have completed LU 1053

Author(s): Amanda Herzog

When Evaluating detection limit we wanted to find out the method and parameter which results in a high recovery at the detection limit (low concentration/large fomite surface area). .

Experimental Design was as follows:

This task involves an experimental evaluation of the detection limit of cultivatable method using *Bacillus thuringiensis* recovered from various fomites. Fomites of interest include plastic, laminar, and stainless steel with surface areas of 0.01 m², 0.1 m². *Bacillus thuringiensis* will be serially diluted in an application medium of water. A total of 50 µL of the sample will be applied to the fomite in a grid formation comprised of fifty 1 µL spots. The method of recovery used will be wiped over the surface in horizontal and vertical strokes on the fomite. Methods of recovery evaluated are the Fellowes Premoistened Surface Cleaning Wipes (48cm²), kimwipe (48cm²) and cotton swab (4 swabs per fomite). Samples are taken at the initial application time and after the samples are dry. In addition humidity and temperature will be monitored. Prewetting will be used before recovering a dry sample to increase recovery, 200 µL of TSB is distributed uniformly using a spreader (the surface and spreader are wiped). 1mL of the extraction solution will be used for cultivation.

Contribution:

We showed the variability of recovery and survival of bacteriophage P22 and *B. thuringiensis* on fomites as a function of fomite type, fomite surface area, application media, relative humidity, wetting agent, recovery materials, time of sampling, and detection method.

Results:

The recovery of bacteriophage P22 and *B. thuringiensis* from fomites, at concentrations near the limit of detection, were most influenced by time of sampling (initial versus dry) and fomite surface area (100 cm² versus 1000 cm²). Differences in recovery were agent specific. An increase in size from 100 to 1000 cm² decreased the recovery by 50 % for bacteriophage P22 and 20 % for *B. thuringiensis*. After the applied samples dried on the fomites, less than 2 % of bacteriophage P22 and 20 % of *B. thuringiensis* was recoverable. The relative humidity affected drying, inactivation, and thus recovery from fomites. With the acute decrease in the recovery from samples dry on the fomite, a TSB wetting agent step was implemented and resulted in an improvement in recovery (approximately 10 %). When comparing the recovery to direct detection of bacteriophage P22, the majority of the loss for sampling times less than 1 hour was due to the poor efficiency of the recovery method (approximately 98 % loss in recovery). The survival of bacteriophage P22 on the fomite (evaluated by direct detection) had significant loss due to inactivation, increasing from approximately 70 % within 2 hours to more than 95 % after one day.

Loss due to recovery vs loss due to decreased infectivity of P22 (799,1053)

Things that are in progress LU 799

Author(s): Amanda Herzog

and Things that I have completed LU 1053

Author(s): Amanda Herzog

When Determining Inactivation we wanted to find out To distinguish between loss due to recovery from loss due to decreased infectivity of P22 on fomites

Experimental Design was as follows:

P22 is grown and serially diluted to various concentrations. For this modified method, P22 drops applied

directly on the 100mm X 15mm plastic petri- dish and left to dry. After the drops were completely dried, 1 ml of TSB added over the dried drops and properly spread using a plastic bacteria spreader. This solution is now as the P22 sample overlaid with mixture of 3ml bacto agar, 1ml TSB and 500 μ L log phase-host cell culture with proper mixing and incubated in inverted position for 18-24 hr at 370C. Plaques were scored for the number of active P22 particles.

Contribution:

We showed the variability of recovery and survival of bacteriophage P22 and *B. thuringiensis* on fomites as a function of fomite type, fomite surface area, application media, relative humidity, wetting agent, recovery materials, time of sampling, and detection method.

Results:

The recovery of bacteriophage P22 and *B. thuringiensis* from fomites, at concentrations near the limit of detection, were most influenced by time of sampling (initial versus dry) and fomite surface area (100 cm² versus 1000 cm²). Differences in recovery were agent specific. An increase in size from 100 to 1000 cm² decreased the recovery by 50 % for bacteriophage P22 and 20 % for *B. thuringiensis*. After the applied samples dried on the fomites, less than 2 % of bacteriophage P22 and 20 % of *B. thuringiensis* was recoverable. The relative humidity affected drying, inactivation, and thus recovery from fomites. With the acute decrease in the recovery from samples dry on the fomite, a TSB wetting agent step was implemented and resulted in an improvement in recovery (approximately 10 %). When comparing the recovery to direct detection of bacteriophage P22, the majority of the loss for sampling times less than 1 hour was due to the poor efficiency of the recovery method (approximately 98 % loss in recovery). The survival of bacteriophage P22 on the fomite (evaluated by direct detection) had significant loss due to inactivation, increasing from approximately 70 % within 2 hours to more than 95 % after one day.

Water Quality Modeling in Potable Water Distribution Systems (252,1089)

Things that are in progress LU 252

Author(s): Christopher Choi

and Things that I have completed LU 1089

Author(s): Christopher Choi

When Modeling dispersion we wanted to find out The primary project goal is to develop and demonstrate a one-dimensional network water quality solver that properly accounts for incomplete mixing of solutes at pipe junctions and for axial dispersion of constituents along pipe links.

Experimental Design was as follows:

programming, experimental verification, benchmarking, code verification

Contribution:

Overall, this study outlines our research efforts aimed at implementing the nodal mixing and dispersive behavior of soluble matter in steady and unsteady pipe flow regimes into the water quality model. We learned that these effects can be significant under various field conditions.

Results:

An accurate water quality modeling tool will be essential for many municipalities that must design or upgrade distribution systems. If network models are to remain effective tools for designing, operating, and managing drinking water distribution systems, it will become necessary to expand existing water quality algorithms so as to properly account for mixing at pipe junctions and unsteady dispersion along pipe links. While these upgrades would present new challenges for water quality modeling in water distribution networks, they would also provide an urgently needed second-generation modeling capability. In this study, we focus primarily on integrating both junction mixing and axial dispersion phenomena with the following steps: First, we use hydraulic calculations in a selected network to provide the database for the water quality simulations that involve incomplete mixing at junctions. Second, we employ a one-dimensional dispersion-advection model, integrated with recently developed coefficients, to produce transient water quality results for the network. The results are then quantitatively compared with those obtained based on the conventional assumptions; i.e., complete mixing and advection-only solute

transport. Accordingly, we have developed AZRED II based on previously developed AZRED I using C++ coding.

Learning Unit Created on 2009-03-04 16:39:38.0 (430,1097)

Things that are in progress LU 430

Author(s): Christopher Choi

and Things that I have completed LU 1097

Author(s): Christopher Choi

When Evaluating risk assessment we wanted to find out impact on public health

Experimental Design was as follows:

modeling

Contribution:

A framework for an event-based risk assessment model of water distribution networks is proposed. An event-based approach was taken in order to gain information about how to better protect networks from contamination events. This is done by describing the portions of the network that are most vulnerable to these contaminations, and these portions should be the focus of those wishing to protect a distribution network from contamination and also mitigate the effects of contaminations that do occur. Sensor placement methods are also investigated, and it is shown that more weight should be given to maximizing the likelihood of detection by placing sensors at optimal locations, rather than by trying to shorten the expected time until detection. It is also shown that optimal sensor placement accomplished using this criterion produces better protection than does increasing in the number of sensors. These findings should be beneficial to utilities planning to install sensor networks and should also encourage rigorous sensor network design as a cost effective way to reduce the impacts of contaminants in a network.

Results:

Traditional risk assessment techniques examine risk of infection or disease in the context of long term risk. The current study takes an event-based approach to evaluating the risk of high impact contamination events. The purpose of this event-based approach is to both evaluate the vulnerability of water distribution systems to such events and to determine the impact that actions taken can have on these events. While *Cryptosporidium* is used as the microbial agent for this study, the results are also intended to provide general information about the characteristics of most other contamination events in water distribution networks. Risk assessment is done using a Monte Carlo framework and simulated events are created using EPANET as the hydraulic and water quality model. To simulate contamination episodes, an exemplary network is used, along with the actions taken by the water utility to mitigate the impact. The reaction to the simulated events is modeled by stopping consumption. A delay is used to represent reaction time in the network. This shows the importance of sensor networks and risk mitigation planning. Sensitivity analysis is also used to indicate the most important parameters in the risk assessment and to indicate which parameters may be further refined so as to improve the model's accuracy.

Modeling and Experimental Verification of Water Distribution Sys (487,1099)

Things that are in progress LU 487

Author(s): Christopher Choi

and Things that I have completed LU 1099

Author(s): Christopher Choi

When Modeling microbial dispersion data we wanted to find out The present EPANET Water Quality model can be drastically improved and the dispersion model can predict the dispersion pattern accurately

Experimental Design was as follows:

Revise EPANET using C/C++ and Delphi based on CFD and experimental data

Contribution:

The models used for predicting water quality in water distribution systems have been subjected to continuous improvement. In the present study, we explored the advantages the might be gained by

integrating axial dispersion and the mixing of solutes that occurs at junctions in pressurized pipe systems.
Results:

A code development to integrate (i) incomplete mixing at junctions and (ii) advection-dispersion-reaction with recently derived dispersion coefficients that exhibited high accuracy for laminar flows.

3. Combined water quality model using mixing and dispersion (877,58)

Things that are in progress unit Number 877

Author(s): Christopher Choi

and Things that I have progress unit Number58

Author(s): Rosina Weber

Initially Modeling transport phenomena we wanted to find out What the most effective search method for learning units is

The original Experimental Design was as follows:

What the most effective search method for learning units is

We are currently trying to find out At present, the prevailing network water quality models are based on two major simplifications. First, solute mixing is assumed to be complete and instantaneous at the pipe junctions. Second, longitudinal dispersion of the solute mass along the pipe axis is ignored, and plug flow is assumed to prevail. However, our recent investigations clearly show that these assumptions are not valid for a wide range of conditions that commonly exist in real pipe networks.

The current Experimental Design is as follows:

1. Evaluate junction mixing and axial dispersion separately. 2. Combine both effects through a single junction. 3. Combine both effects through multiple junctions. 4. Conduct experimental verification. 5. Build contamination scenarios.

Detection Limits All Methods for Respiratory and Foodborne Virus (1083,909)

Things that are in progress unit Number 1083

Author(s): Amanda Herzog

and Things that I have progress unit Number909

Author(s): Amanda Herzog

Initially Evaluating detection limit we wanted to find out the detection limit for all methods detecting influenza

The original Experimental Design was as follows:

The detection limit for all methods detecting influenza

We are currently trying to find out The detection limit for all methods detecting respiratory and foodborne viruses and the risk estimates at those detection limits.

The current Experimental Design is as follows:

Literature from published journal articles on the detection methods for the organisms of interest will be reviewed. Journal articles will be collected using a number of key words on ISI Web of Science.

References will be exported into an EndNote file. A manual screening will be conducted to eliminate any references that were not expected to contain relevant data.

Improvement of Risk Assessment for Bacillus anthracis (1084,910)

Things that are in progress unit Number 1084

Author(s): Amanda Herzog

and Things that I have progress unit Number910

Author(s): Amanda Herzog

Initially Evaluating detection limit we wanted to find out the environmental detection limit and parameters which may affect recovery of the sample.

The original Experimental Design was as follows:

The environmental detection limit and parameters which may affect recovery of the sample.

We are currently trying to find out the environmental detection limit and parameters which may affect

recovery of the sample.

The current Experimental Design is as follows:

The risk assessment approach presented in the manuscript, Implications of Limits of Detection of Various Method for *Bacillus anthracis* in Computing Risks to Human Health, could be further improved if an experimental probability distribution of the estimated dose was available. To obtain such a distribution, a large number of different true doses must be spiked in the environmental matrix interest and the sample processed through an entire protocol. For this evaluation *B. thuringiensis* will be spiked into soil with various characteristics. Parameters affecting the recovery and detection will be evaluated. Various extraction and processing methods will be evaluated. Samples will be evaluated using qPCR, LAMP, MySelect, or cultivation.

454 Sequencing of Highly Touched and Untouched Fomites. (1086,731)

Things that are in progress unit Number 1086

Author(s): Amanda Herzog

and Things that I have progress unit Number 731

Author(s): Amanda Herzog

Initially Analyzing Availability of DNA we wanted to find out the make up of background bacterial populations at touched and untouched surfaces as illustrated by their 16S rRNA gene.

The original Experimental Design was as follows:

the make up of background bacterial populations at touched and untouched surfaces as illustrated by their 16S rRNA gene.

We are currently trying to find out the genetic characterization of background bacterial populations on touched and untouched surfaces as illustrated by their 16S rRNA gene.

The current Experimental Design is as follows:

Samples will be provided by the Influenza Fomite Sampling Project from the University of Michigan.

Samples will be taken from highly touched and untouched fomites in dormitories. DNA samples will be amplified with PCR, run on gel and purified with PCR purification kit. Samples will be processed to extract DNA. DNA will be evaluated for its quality and quantity. 16S rRNA genes will be amplified by using universal primers with 454 associated tags. Primers will be designed to target conserved regions surrounding hypervariable regions of relevant genes, and amplicons will be used for sequencing.

Amplified 16S rRNA genes will be purified. Purified 16S genes will be given to Research Technology Support Facility (RTSF) for the sequencing on 454 of 16S rRNA genes.

8. Outputs:

1. Students Supported:

Amanda Herzog, supervisor: Dr. Syed Hashsham.

Prianca Bhaduri (2010 summer semester), supervisor: Dr. Syed Hashsham.

Ryan Austin, supervisor: Dr. Christopher Choi

Pedro Romero, supervisor: Dr. Christopher Choi

Emily Kaufman, supervisor: Dr. David M. Wagner

Heather Papinchak, supervisor: Dr. Mark Nicas

Jerry Lopez, supervisor: Dr. Charles Gerba

2. Students Graduated:

Dieter Tourlousse completed his PhD degree in August 2010 under the supervision of professor Syed Hashsham from Civil and Environmental Engineering at Michigan State University. Dissertation thesis titled: Development of Low-Cost and Easy-to-Use Tools for Multiplex Pathogen Detection.

Pedro Romero-Gomez, supervisor: Dr. Christopher Choi. Dissertation Title: Transport phenomena in drinking water systems, May 2010, the University of Arizona.

3. Publications:

Amanda B. Herzog, Alok K. Pandey, Prianca Bhaduri, Charles P. Gerba 2, Joan B. Rose, and Syed A. Hashsham. Bacteriophage P22 and *B. thuringiensis* Fomite Recovery Manuscript submitted to Applied and Environmental Microbiology titled "Evaluation of Recovery Efficiency and Survival of Bacteriophage P22 and *Bacillus thuringiensis* on Fomites" (AEM02584-10 Version 1)

Greenberg, D.L., J.D. Busch, D.M. Wagner, and P. Keim. 2010. Identifying experimental surrogates for *Bacillus anthracis* spores: a review. *Investigative Genetics* 1:4

Spicknall IH, JS Koopman, M Nicas, JM Pujol, L Sheng and JNS Eisenberg (2010): Informing optimal environmental influenza interventions: how the host, agent, and environment alter dominant routes of transmission, *PLoS Computational Biology*, Volume 6(10): e1000969. doi:1371/journal.pcbi.1000969

Romero-Gomez, P., K. E. Lansey, C. Y. Choi, 2010, Impact of an incomplete solute mixing model on sensor network design, *Hydroinformatics* (web version available; in press)

Romero-Gomez, P. and C. Y. Choi, 2010, Axial dispersion coefficients in laminar flows of water distribution systems, *ASCE Journal of Hydraulic Engineering* (accepted upon revision, revision underway).

4. Patents:

5. Presentations:

Michigan Branch ASM Meeting

Poster presentation titled "Evaluation of Recovery Efficiency and Survival of Bacteriophage P22 and *Bacillus thuringiensis* on Fomites". Michigan Branch of the American Society for Microbiology Fall meeting "Microbiology Method for Education and Exploration" on October 8-9, 2010.

Romero-Gomez, P., D. Kang, G. Wood, C. Y. Choi, 2010. A Game Theory Approach for Decentralization of Reclaimed Water Systems, *Water Distribution Systems Analysis (WDSA)*, Tucson, AZ.

Austin, R. G., C. Y. Choi, P. L. Gurian, T. C. Balagopal, 2010, Event-Based Microbial Risk Assessment and Response Analysis of *Cryptosporidium* in Municipal Water Distribution Networks, *Water Distribution Systems Analysis (WDSA)*, Tucson, AZ.

Andrade, M. A., F. Rojano, P. Romero-Gomez, and C. Y. Choi, 2010, Integrated Water Quality Modeling of Water Distribution Systems, *Water Distribution Systems Analysis (WDSA)*, Tucson, AZ.

6. Organization of workshops:

7. Participation in workshops:

IWA QMRA Workshop materials prepared by Pedro Romero and Chris Choi. It is presented by Mark Weir at IWA World Water Congress and Exhibition in Montreal, Canada. 9/19-9.24, 2010.

8. Case studies algorithms developed:

AZRED II – Advanced Water Quality Modeling Software developed at the University of Arizona. The theory is developed by Pedro Romero-Gomez, and it is verified with experimental data collected by Ryan Austin. Alex Andrade developed the code, AZRED II, using C/C++ under the supervision of Chris Choi.

9. Algorithms developed:

10. Human Resource Development:

11. Funds Leveraged (additional funding. resources for free):

9. Outcomes:

Unit 863: Improvement of QMRA methods through more detailed exposure assessment methods.

Unit 877: The primary goal of this research is to improve our ability to understand, model, predict and

therefore better control water quality in potable water distribution systems. Therefore we intend to focus on refining a valuable but outdated network water quality solver to include incomplete mixing at pipe junctions and axial dispersion of soluble constituents.

Unit 909: Risk assessors will have better knowledge about methods detecting influenza

Unit 910: Risk assessors will have better knowledge about environmental detection limit and recovery.

Unit 918: Model validation in predicting solute transport thorough a series of tracer experiments in a pressurized 5x5 network with 9 cross junctions

Unit 1053: First responders will have better knowledge of the affect of certain parameters on recovery and survival of bacteriophage P22 and *B. thuringiensis* on the fomites.

Unit 1083: Risk assessors will have better knowledge about methods detecting respiratory and foodborne viruses.

Unit 1084: Risk assessors will have better knowledge about environmental detection limit and recovery

Unit 1086: Occurrence data for bacterial populations and presence of bacterial pathogens.

Unit 1089: Compilable, user-friendly water quality code - AZRED II

Unit 1097: A few well placed sensors can be a good solution, but more care may be required when deciding the sensors' locations.

Unit 1099: AZRED II

Unit 1100: Verification of AZRED II using experimental data sets in water systems networks

Unit 1101: Better risk assessment using an improved water quality model

10. Integration with other projects:

An association was created between Unit 469, authored by Patrick Gurian (Project IV, Drexel University) and Unit 478, authored by Mark Nicas (Project I, U of California Berkeley)

An association was created between Unit 484, authored by Rachael Jones (Project I, U of California Berkeley) and Unit 481, authored by Shamia Hoque (Project III, Drexel University)

An association was created between Unit 481, authored by Shamia Hoque (Project III, Drexel University) and Unit 487, authored by Christopher Choi (Project I, U of Arizona)

An association was created between Unit 579, authored by David Greenburg (Project I, Northern Arizona U) and Unit 490, authored by Christopher Choi (Project I, U of Arizona)

An association was created between Unit 476, authored by Mark Nicas (Project I, U of California Berkeley) and Unit 519, authored by Ian Spicknall (Project II, U of Michigan)

An association was created between Unit 58, authored by Rosina Weber (Project V, Drexel University) and Unit 877, authored by Christopher Choi (Project I, U of Arizona)

11. Anticipated Technical Results and Developments:

Project II Report by Joseph Eisenberg

CAMRA Report for Year V (15 Sept 2009 to 14 Sept 2010) for Project II

1. Project II
2. Investigators: Joe Eisenberg, James Koopman, Josep Pujol, Ian Spicknall, Sheng Li, Nottasorn Plipat, Bryan Mayer, Jijun Zhao
3. Project Goals:
4. Tasks for Year V (15 Sept 2009 to 14 Sept 2010):
 - 1.) Continue development of the Environmental Infection and Transmission System (EITS) models. Main focus during Year 5 will be to examine the impact of behavior and movement patterns on the transmission of Influenza and ultimately on risk.
 - 2.) Finalize dose timing dose response model analysis, using multiple dosing data from an Anthrax observational study with monkeys.
 - 3.) Application of EITS for:
 - a. Examining the impact of realistic interventions (hand hygiene, masks, decontamination, and cough etiquette) on minimizing risk.
 - b. Examining the impact of social structure on the indirect risks associated with outbreaks.
 - c. Examining the risk of MSRA in hospital settings, developing of a detailed realistic EITS model for the surgical intensive care unit (SICU) at the University of Michigan hospital, and examining the effects of cleaning and decontamination in the SICU.
 - d. Examining the impact of decontamination of desktops in schools on minimizing absenteeism.

5. Research Activities

Researcher Name	Research Activity
Sheng Li	Developing models Modeling transmission
Nottasorn Plipat	Analyzing data analysis Reviewing knowledge Analyzing data Modeling transmission
Bryan Mayer	Estimating dose response
Jijun Zhao	Analyzing transmission

6. Background and prior research:
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. Model and Analysis of Multiple Influenza Routes Things that are in progress LU (1106)

Author(s): Jijun Zhao

When Analyzing transmission we wanted to find out under different venue situations, which route contribute more and what cause the different results for different situations.

Experimental Design was as follows:

1. Establish ODE model of multiple routes including aerosol route and fomite routes. 2. Derive R_0 of the whole system and of each of the routes and write into general form if possible. 3. Analyze which transmission stage is more important for different route under different venue settings: 1) shedding and contamination of route; 2) picking up and elimination of pathogens from route environment; for fomite routes, there is a third factor group, 3) human behavior after pathogens being picked up.
2. Anthrax Cumulative Dose Response Estimation (336,820)

Things that are in progress LU 336

Author(s): Bryan Mayer

and Things that I have completed LU 820

Author(s): Bryan Mayer

When Fitting data we wanted to find out how does probability of infection (symptoms, or death) change when we analyze data that uses multiple dosing as opposed to a bolus dose?

Experimental Design was as follows:

A study was conducted in 1966 on inhalation anthrax using an observational animal study. Monkeys were placed in a wool sorting mill and received continuous exposure to aerosolized anthrax. We are using these data to fit our three parameter cumulative dose response model (manuscript in preparation; Pujols, Eisenberg, and Koopman) which incorporates pathogen growth and immune response in addition to the standard exponential model risk parameter.

Contribution:

The need for more specific data concerning time-dependent exposure events. Specifically, time to infection and ranges for host clearance for specific pathogens. Furthermore, controlled experiments will be required to understand if dose timing and dose order are important for risk estimation.

Results:

By fitting time-dependent dose-response model to Brachman data we were able to identify potential parameters settings to describe dose clearance within host. Also, further experimental needs were identified.

ODE Model and Analysis of the Dominance of Influenza Routes (924,1103)

Things that are in progress LU 924

Author(s): Jijun Zhao

and Things that I have completed LU 1103

Author(s): Jijun Zhao

When Modeling transmission we wanted to find out 1) The clear process of transmission. 2) How will individual behaviors and venue characteristics affect the risk of influenza and to what extent? 3) What kind of interventions related to different environments will be more effective to reduce the risk of influenza? 4) How will types of environments influence the relative importance of transmission routes. 5) What are the important parameters that are need to understand the routes?

Experimental Design was as follows:

- 1) Literature review of the influenza transmission processes, routes and experimental results of related parameters. 2) Development of conceptual model of the whole transmission system and ODE models of each transmission route. 3) Mathematical analysis of the contributions of transmission routes, and effects of model parameters on the dominances. 4) Analysis of dynamics of every transmission route and the dynamics of whole transmission system. 5) Determination of effective interventions for key transmission

processes.

Contribution:

By distinguishing the fomite mediated routes through the ways that fomites are contaminated, we can understand how human behaviors and fomite characteristics affect the relative strength of fomite mediated route, how source of contamination (through hands or coughs and sneezes) would affect the transmission, and what other factors increase and decrease transmission via fomite mediated routes.

Results:

Fomite mediated influenza transmission is modeled as two routes according to the contamination source of the fomite: hand-contaminated or droplet-contaminated fomites. Basic reproduction number (R_0) formulations for these routes are derived and divided into separate processes of excretion, contamination, pickup, and self inoculation leading to infection. The relative contributions of the two routes on the total fomite influenza transmission are compared by using the ratio of the R_0 s for two situations: shedding either on hands or fomite, shedding to the clothes on upper arm. The effects of control measures on R_0 are compared for fomites from which pathogens have higher or lower fractions that are picked up by hands and from which the fomite is highly or lowly contaminated.

Assessment of MRSA acquisition in intensive care unit (874,1108)

Things that are in progress LU 874

Author(s): Nottasorn Plipat

and Things that I have completed LU 1108

Author(s): Nottasorn Plipat

When Analyzing data analysis we wanted to find out the model conditions at which it will generate similar observed hazard relationship as in the observed data.

Experimental Design was as follows:

1) Describe patterns and distributions of variables associated with MRSA transmission. This variables include 1.1) individual level factors (age, gender, previous hospitalization and 1.2) contextual factors, which are 1.2.1) environmental (rooms and ICU) level factors (such as previous room occupant MRSA status, number of previous vacant room-days prior to admission, and ICU colonization pressure) and 1.2.2) variables related to health care workers 2) Describe daily hazard of MRSA acquisition and perform survival analysis to understand the effects of these variables to the hazard 3) Develop an environmentally mediated infection transmission model for MRSA transmission in the SICU 4) Use these observed data to constrain the model parameters

Contribution:

Vacant room time might generate increased MRSA acquisition risk through multiple mechanisms. Shorter time may reflect smaller opportunity for quality cleaning. It may also imply increased nursing workload. These factors are various indirect measures of the underlying dynamic of patient's environments in space and time that effect the acquisition risks. Inferences from our study are limited by the small number of acquisitions. But we hope our observation of an association of shorter vacant room time and MRSA acquisition in an ICU, where strict infection control strategy was implemented, will stimulate more careful attention to this issue in other studies.

Results:

We analyzed environmental risks associated with new MRSA acquisition in a surgical ICU. These risks were exposure to rooms previously occupied by MRSA positive patients and vacant room time prior to room occupancy. Our findings indicate that a shorter vacant room time between patient admissions was associated with MRSA acquisition. The vacant room time prior to occupancy was almost 50% longer in patients who did not acquire compared to those who did. When those who acquired MRSA are divided into those who acquired early and those who acquired later, the association is stronger for those who acquired early. We observed only a small and statistically insignificantly higher acquisition of MRSA in people whose prior room occupant was MRSA positive compared to those whose prior occupant was negative.

3. Assessment of MRSA acquisition in intensive care unit (874,397)

Things that are in progress unit Number 874

Author(s): Nottasorn Plipat

and Things that I have progress unit Number397

Author(s): Nottasorn Plipat

Initially Analyzing data analysis we wanted to find out environment role in the transmission of MRSA

The original Experimental Design was as follows:

Environment role in the transmission of MRSA

We are currently trying to find out We would like to explore the model conditions at which it will generate similar observed hazard relationship as in the observed data.

The current Experimental Design is as follows:

1) Describe patterns and distributions of variables associated with MRSA transmission.

This variables include 1.1) individual level factors (age, gender, previous hospitalization

and 1.2) contextual factors, which are 1.2.1) environmental (rooms and ICU) level

factors (such as previous room occupant MRSA status, number of previous vacant

room-days prior to admission, and ICU colonization pressure) and 1.2.2) variables

related to health care workers 2) Describe daily hazard of MRSA acquisition and

perform survival analysis to understand the effects of these variables to the hazard 3)

Develop an environmentally mediated infection transmission model for MRSA

transmission in the SICU 4) Use these observed data to constrain the model parameters

MRSA environmentally mediated infection transmission model (876,874)

Things that are in progress unit Number 876

Author(s): Nottasorn Plipat

and Things that I have progress unit Number874

Author(s): Nottasorn Plipat

Initially Reviewing knowledge we wanted to find out the model conditions at which it will generate similar observed hazard relationship as in the observed data.

The original Experimental Design was as follows:

We would like to explore the model conditions at which it will generate similar observed hazard relationship as in the observed data.

We are currently trying to find out 1) model parameters and their ranges 2) model behaviors under different scenarios. Ultimately, we would like to know from this preliminary model what model parameters are critical in the transmission process that will need further study. We also want to gain insight into how the physical environments and health care workers interact and their effects on the transmission outcome.

The current Experimental Design is as follows:

1) develop the conceptual environmentally mediated infection transmission model of MRSA in SICU.

This includes patient's environment and contacts with health care workers. 2) review of the literature for the parameters that will be used in the model 3) develop an agent based model for the 20

bed SICU

Hand and environmental mediated transmission of MRSA (1109,876)

Things that are in progress unit Number 1109

Author(s): Nottasorn Plipat

and Things that I have progress unit Number876

Author(s): Nottasorn Plipat

Initially Modeling transmission we wanted to find out 1) model parameters and their ranges 2) model behaviors under different scenarios. Ultimately, we would like to know from this preliminary model what model parameters are critical in the transmission process that will need further study. We also want

to gain insight into how the physical environments and health care workers interact and their effects on the transmission outcome.

The original Experimental Design was as follows:

1) model parameters and their ranges 2) model behaviors under different scenarios. Ultimately, we would like to know from this preliminary model what model parameters are critical in the transmission process that will need further study. We also want to gain insight into how the physical environments and health care workers interact and their effects on the transmission outcome.

We are currently trying to find out Health care worker's hands and hospital environments are both significant contributors to transmission of MRSA colonization. Hands are vectors of transmission introducing new acquisitions into new and clean rooms, while environments are pathogen reservoir for further acquisitions in already contaminated rooms. We would like to use the model to describe hand mediated and environmental mediated transmission routes of MRSA colonization in hospital environments both clean and contaminated rooms.

The current Experimental Design is as follows:

1) Literature review for model parameters 2) Develop a simple conceptual model for hand and environmental mediated transmission of MRSA colonization in a hospital environment 3) Develop a corresponding individual based model for the conceptual model 4) Simulation of various scenarios 5) Simulated data analysis to describe hand mediated and environmental mediated transmission routes

4. The effects of movement patterns on flu transmission modes (372,857)

Things that are in progress unit Number 857

Author(s): Sheng Li

and Things that I have completed unit Number 372

Author(s): Sheng Li

Once we learned:

These insights provide a theoretical context to examine the role of the environment in pathogen transmission; and our modeling framework provides a means to interpret environmental data to inform environmental interventions.

This result led us to the following research question Developing models we wanted to find out 1)How venue structure and movement pattern in venues affects the relative importance of four transmission modes (frequently touched fomites, infrequently touched fomites, inspirable airborne, respirable airborne) 2) How venue structure and movement in venue structure alters the single and joint effects of four transmission modes. 3) What specific venue structure abstractions have large enough effects so that they must be considered in realistic models 4) Which specific movement abstractions have large enough effects so that they must be considered in realistic models 5) how superspreaders alter the effects of four transmission modes

The current Experimental Design is as follows:

1) Do literature review to summarize the important fomit type, movement patterns and venue structure, and then conceptualize the characteristics for our theoretical agent-based model. 2) Develop an agent-based model with various human movement patterns in Java. 3) Verify the model. 4) Model parameter exploration and model simulation analysis.

ODE Model and Analysis of the Dominance of Influenza Routes (372,859)

Things that are in progress unit Number 859

Author(s): Sheng Li

and Things that I have completed unit Number 372

Author(s): Sheng Li

Once we learned:

These insights provide a theoretical context to examine the role of the environment in pathogen transmission; and our modeling framework provides a means to interpret environmental data to inform

environmental interventions.

This result led us to the following research question Modeling transmission we wanted to find out 1) The clear process of transmission. 2) How will individual behaviors and venue characteristics affect the risk of influenza and to what extent? 3) What kind of interventions related to different environments will be more effective to reduce the risk of influenza? 4) How will types of environments influence the relative importance of transmission routes. 5) What are the important parameters that are need to understand the routes?

The current Experimental Design is as follows:

1) Literature review of the influenza transmission processes, routes and experimental results of related parameters. 2) Development of conceptual model of the whole transmission system and ODE models of each transmission route. 3) Mathematical analysis of the contributions of transmission routes, and effects of model parameters on the dominances. 4) Analysis of dynamics of every transmission route and the dynamics of whole transmission system. 5) Determination of effective interventions for key transmission processes.

8. Outputs:

1. Students Supported:

Ian Spicknal

Sheng Li

Nottasorn Pilat

Bryan Mayer

2. Students Graduated:

3. Publications:

Mayer B.T., Koopman J.S., Ionides E.L., Pujol J.M., Eisenberg J.N.S. (In Press) A Dynamic Dose-Response Model to Account for Exposure Patterns in Risk Assessment: A Case Study in Inhalation Anthrax. Proceedings of the Royal Society: Interface.

Spicknall I.H., Koopman J.S., Nicas M., Pujol J.M., Li S., Eisenberg J.N.S. (2010) Informing Optimal Environmental Influenza Interventions: How the Host, Agent, and Environment Alter Dominant Routes of Transmission 6(10). PLoS Computational Biology

Zelner J., King, A.A., Moe C.L., Eisenberg, J.N.S (2010) How Infections Propagate After Point Source Outbreaks: An Analysis of Secondary Norovirus Transmission. 21(5) Epidemiology

4. Patents:

5. Presentations:

Spicknall, I.H. Eisenberg, J.N.S. Dominant Modes of Influenza Transmission: An Epidemiologic Perspective. 2010 Joint Conference of International Society of Exposure Science International Society for Environmental Epidemiology, Seoul South Korea

Mayer B. Presentation to the Environmental Protection Agency, Homeland Security, and CAMRA regarding work on time-dependent dose-response modeling results on anthrax infection in monkeys.

6. Organization of workshops:

7. Participation in workshops:

8. Case studies algorithms developed:

9. Algorithms developed:

10. Human Resource Development:

11. Funds Leveraged (additional funding, resources for free):

9. Outcomes:

Unit 820: Exposure patterns may be an important component of dose-response risk estimation.

Unit 857: 1) Identify venue and movement abstractions that can have large effects so as to focus the abstraction of complex reality on these 2) Specify the conditions (such as population density) which alter the importance of these venue and movement abstractions so as to again focus the abstraction of reality on what makes a difference 3) explain How superspreaders alter the importance of these venue and movement abstractions

Unit 859: 1) Parameter ranges that will yield specific system behaviors. 2) Analysis measures for relative importance of routes when related parameter ranges are known. 3) Analysis measures for relative contributions of routes under different environmental settings. 4) Results that might be applied for helping decision making.

Unit 1067: 1) The temporal dynamic of the relative importance of respiratory transmission mode partially depends on respirable viral particles environmental persistence and dispersion processes. 2) Super spreader influences the relative importance of respiratory transmission mode and final fraction of infection in influenza epidemics. 3) Movement pattern changes the relative importance of respiratory transmission mode and final fraction of infection in influenza epidemics. 4) The decision of effective intervention should consider temporal pattern of respiratory transmission mode.

Unit 1103: 1. Droplet-contaminated and hand-contaminated fomite routes are distinguished by processes of the infected individual's shedding and deposition to the environment. 2. Conditions where transmissions from hand-contaminated fomites could exceed transmissions from droplet-contaminated fomites are distinctly unusual. 3. Covering a cough using the upper arm rather than hand would decrease total fomite routes transmission, while cover a cough by hands would only decrease droplet-contaminated fomite transmission and not necessarily decrease total fomite transmission. 4. Transmissions through fomites are sensitive to shedding amount and also to the extent of the fomite contamination through shedding and touching. 5. Measures related to pathogen pickup and elimination on a fomite are fomite type sensitive: they are not useful for fomites that have low pickup rate but are efficient for fomites that have high pickup rate. 6. Measures after pathogens being picked up, for example hand hygiene would decrease transmission to some extent.

Unit 1106: Find out interactions of transmission stages (or factors) for influenza transmission with multiple routes.

Unit 1108: Shorter vacant room time on admission is associated with MRSA acquisition.

Unit 1109: Hand mediated transmission is dominant in the initial acquisitions of new and clean rooms. Environmental mediated transmission is dominant in subsequent acquisitions of contaminated rooms.

10. Integration with other projects :

An association was created between Unit 372, authored by Sheng Li (Project II, U of Michigan) and Unit 426, authored by Scott McLennan (Project IV, Michigan State U)

An association was created between Unit 476, authored by Mark Nicas (Project I, U of California Berkeley) and Unit 519, authored by Ian Spicknall (Project II, U of Michigan)

An association was created between Unit 748, authored by Ian Spicknall (Project II, U of Michigan) and Unit 762, authored by Patrick Gurian (Project IV, Drexel University)

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

Project III Report Charles N. Haas

CAMRA Report for Year V (15 Sept 2009 to 14 Sept 2010) for Project III

1. Project III
2. Investigators: Chuck Haas, Carole Bolin, Yin Huang, Sushil Tamrakar, Shamia Hoque, Sondra Teske
3. Project Goals:
4. Tasks for Year V (15 Sept 2009 to 14 Sept 2010):

Dr. Charles N. Haas' Laboratory (Drexel University)

Administrative:

- 1.) Assist director with overall management tasks and scientific leadership.
- 2.) Work with director to interface with US EPA, DHS and other external constituents.
- 3.) Assist director with coordination of cross-project activities.

Modeling:

- 1.) Mechanistic model of multiple exposure routes and interspecies relationships
- 2.) Mechanistic incorporation of time post inoculation for *Bacillus anthracis* (*B. anthracis*), *Francisella tularensis* (*F. tularensis*) and *Yersinia pestis* (*Y. pestis*).
- 3.) Collaboration with Project II on coupling of dose response time models to population models.
- 4.) Modeling multiple dosing *F. tularensis* data when made available from Michigan State University (MSU).
- 5.) Kinetics modeling of multiple dosing data when made available from MSU.
- 6.) Verification of mechanistic basis of time-dose response model, demonstrating use to predict *in-vivo* bacterial kinetics based on host response will be finalized.
- 7.) A paper that estimates the dose-dependent incubation distribution of inhalation anthrax based on animal data and shows a consistency of the prediction for low-dose response with human data from Sverdlovsk outbreak will be finalized.
- 8.) Time to response for avian influenza A (H5N1) infection.
- 9.) Study infectious effect on hamsters exposed repeatedly to scrapie agent.
- 10.) In collaborative work with Project IV, combining dose-response analysis and stochastic human exposure models, for estimating the impact of human behaviors and transfer coefficients on the probability of infection caused by an intentional release of *Norovirus*.
- 11.) Collaboration with Project IV to integrate the time-dose-response model with an ordinary differential equation system that predicts the fate and transport of various Category A biological agents, in order to estimate the infection dynamics of a population exposed to those agents in an indoor environment.
- 12.) Multiple routes exposure and interspecies relationships of *Rickettsial* diseases such as Rocky Mountain spotted fever and murine typhus.
- 13.) Mechanistic dose response model will be developed for *Brucella* species (including *B. melitensis*, *B. suis*, and *B. abortus*)
- 14.) Post exposure time dependence of dose response for *Brucella* will be completed, with cross-comparisons to outbreak data.
- 15.) Continuing the work on outbreak data validations for different pathogens.

Dr. Carol Bolin's Laboratory (Michigan State University)

1.) Continue multiple dosing animal model experiments with *F. tularensis*

5. Research Activities

Researcher Name	Research Activity
Yin Huang	Modeling dose response Validating dose response model Advancing dose response model
Sushil Tamrakar	Collecting data Developing dose response Developing dose response model
Carole Bolin	Determining dose response
Sondra Teske	Developing dose response model Developing environment Analyzing epidemiologic outbreak
Charles N. Haas	Gathering data

6. Background and prior research:

Things I have read Learning Unit number 729

1-Lundgren, D. L. and B. D. Thorpe (1966). "Infectious Diseases in Wild Animals in Utah: VII. Experimental Infection of Rodents with *Rickettsia rickettsii*." *American Journal of Tropical Medicine and Hygiene* 15(5): 799-806. 2-Kenyon, R. H., R. A. Kishimoto and W. C. Hall (1979). "Exposure of guinea pigs to *Rickettsia rickettsii* by aerosol, nasal, conjunctival, gastric, and subcutaneous routes and protection afforded by an experimental vaccine." *Infection and Immunity* 25(2): 580-582. 3-Saslaw, S. and H. N. Carlisle (1966). "Aerosol infection of monkeys with *Rickettsia rickettsii*." *Bacteriological Reviews* 30(3): 636-645. 4-Sammons, L. S., R. H. Kenyon, G. T. Burger, C. E. Pedersen and R. O. Spertzel (1976). "Changes in blood serum constituents and hematologic values in *Macaca mulatta* with Rocky Mountain spotted fever." *American Journal of Veterinary Research* 37(6): 725-730. 5- Gonder, J. C., R. H. Kenyon and C. E. Pedersen, Jr. (1979). "Evaluation of a killed Rocky Mountain spotted fever vaccine in cynomolgus monkeys." *Journal of Clinical Microbiology* 10(5): 719-723. 6-DuPont, H. L., R. B. Hornick, A. T. Dawkins, G. G. Heiner, I. B. Fabrikant, C. L. J. Wissemann and T. E. Woodward (1973). "Rocky Mountain spotted fever: a comparative study of the active immunity induced by inactivated and viable pathogenic *Rickettsia rickettsii*." *The Journal of Infectious Diseases* 128(3): 340-344.

Things I have read units entered by Sushil Tamrakar

Things I have read Learning Unit number 1020

Explore data set and compile information from suitable data source.

Druett H A, Henderson DW, Peacock S. Studies on Respiratory Infection. III. Experiments with *Brucella suis*. *The Journal of Hygiene*, 1956; 54(1): 49-57. Elberg SS. and Henderson DW. Respiratory Pathogenicity of *Brucella*. *The Journal of Infectious Diseases*, 1948; 82(3): 302-306. Elberg SS, Henderson DW, Herzberg M, Peacock S. Immunization against *Brucella* infection IV. Response of monkeys to injection of a streptomycin-dependent strain of *Brucella melitensis*. *Journal of Bacteriology*, 1955; 69 (6): 643-648.

Things I have read Learning Unit number 1027

Aerosol diameter size can affect the dose-response relationship.

Day WC, Berendt RF. (1972) Experimental Tularemia in *Macaca mulatta*: Relationship of aerosol particle size to the infectivity of airborne *Pasteurella tularensis*. *Infection and Immunity* 5 (1): 77-82.

Things I have read units entered by Sondra Teske

7. Research Contributions this Year:

1. Dose-Response Model of Rocky Mountain spotted fever (RMSF) Things that are in progress LU (1009)

Author(s): Sushil Tamrakar

When Developing dose response we wanted to find out if aerosol exposed rhesus monkeys and intrademally inoculated human can be described by the same dose-response model.

Experimental Design was as follows:

- 1- Mining the usable data, 2- Test for dose-response trend 3- Develop dose-response models 4- Evaluate best fit model 5- Low dose extrapolation

Dose-Response Model of Murine Typhus (*Rickettsia typhi*) Things that are in progress LU (1017)

Author(s): Sushil Tamrakar

When Developing dose response model we wanted to find out: 1) Dose-response model 2) Time post inoculation model 3) Age dependency

Experimental Design was as follows:

- 1- Mining the usable data, 2- Test for dose-response trend 3- Develop dose-response models 4- Evaluate best fit model 5- time post inoculation analysis 6- age dependency analysis

Animal and Human Dose Response Models for *Brucella* species Things that are in progress LU (1022)

Author(s): Sondra Teske

When Developing environment we wanted to find out whether different data sets, and different routes of administration, or between subject species can be successfully pooled into defensible, comprehensive dose response model.

Experimental Design was as follows:

Exploring data, developing dose response models, pooling data, analyzing the results

Comparison of animal-derived incubation with human outbreak data Things that are in progress LU (1058)

Author(s): Yin Huang

When Validating dose response model we wanted to find out if the animal-derived inhalation anthrax incubation distributions will be consistent with human epidemiological data from outbreaks

Experimental Design was as follows:

We will firstly collect the available time-to-response data of inhalation anthrax from animal studies and human outbreak. We will then review and expand a class of time-dose-response models to model theoretically the dose-dependent incubation time-to-response distribution. We will show the findings of the best-fit evaluation and parameter estimation for the candidate models fit to the animal data, and compare the predictions of low-dose incubation distribution based on the best-fit model with the outbreak data for verification.

The relationship between bacterial kinetics and host response Things that are in progress LU (1059)

Author(s): Yin Huang

When Validating dose response model we wanted to find out a direct verification of the biological validity of the time-dose-response models with in vivo pathogen growth.

Experimental Design was as follows:

Open literature will be searched for survival dose-response data and bacterial viable count data for

monkeys infected by *F. tularensis* via inhalation route. The time-dose-response models by Huang et al. will be further developed to model quantitatively the hypothetical relationship between the host response and instantaneous microorganism number in vivo. The resulting models will be fit to survival dose-response data and the estimates of bacterial dynamics for different aerosol sizes were inferred. The estimates will then be compared with the data of bacterial growth and the clinical and pathological findings for verification.

2. Dose-Response Model for *Coxiella burnetii* (Q fever) (311,1008)

Things that are in progress LU 311

Author(s): Sushil Tamrakar

and Things that I have completed LU 1008

Author(s): Sushil Tamrakar

When Developing dose response model we wanted to develop dose-response model for Q fever

Experimental Design was as follows:

1- Mining the usable data, 2- Test for dose-response trend 3- Develop dose-response models 4- Evaluate best fit model 5- Low dose extrapolation.

Contribution:

The animal models presented in this study represent a rare mode of infection. To predict the risk of human infection, experimental data on aerosol exposure-response data are required. Estimating the risk for secondary transmission would require additional data on the period during which infected persons produce aerosols with infectious *C. burnetii* and the fate and transport of *C. burnetii* in various environments. The results of these studies would be invaluable for advancing our understanding of the transmission of infectious agents in the population.

Results:

Based on the differences in the dose-response models $i_{1/2}$ fit to the data for different strains of mice, SCID mice were clearly more sensitive to intraperitoneal exposure to *C. burnetii* than the C57BL/6J and C57BL/10ScN mice. The 50% average lethal dose (LD50) for SCID mice was 2,302 organisms, whereas the LD50 doses were 1.26×10^{10} and 2.83×10^7 for the C57BL/6J and C57BL/10ScN mice respectively. A level of risk of 1/10, 0000, corresponding doses for C57BL/6J mice and C57BL/10ScN will be 1755 and for 231 organisms respectively. As immunodeficiency is a major factor in the development of chronic Q fever, the dose-response model for SCID mice might be a good model to study. The route of infection has vital role in determining minimum inoculum size, the severity of the disease and clinical manifestations.

Dose-Response Model of Murine Typhus (*Rickettsia typhi*) (1017,1018)

Things that are in progress LU 1017

Author(s): Sushil Tamrakar

and Things that I have completed LU 1018

Author(s): Sushil Tamrakar

When Developing dose response model we wanted to find out 1) Dose-response model 2) Time post inoculation model 3) Age dependency

Experimental Design was as follows:

1- Mining the usable data, 2- Test for dose-response trend 3- Develop dose-response models 4- Evaluate best fit model 5- time post inoculation analysis 6- age dependency analysis

Contribution:

Intradermally or subcutaneously inoculated rats (adult and newborn) models suggest that less than 1 PFU (1.33 to 0.38 in 95 % confidence limits) of the pathogen is enough to seroconvert 50 % of the exposed population in an average. BALB/c mouse: the time post inoculation model also indicates that an average dose of 0.28 PFU (0.75 to 0.11 in 95% confidence limits) will seroconvert 50% of exposed

mice

Results:

Dose-response models of different host age of rats and time post inoculation effect in BALB/c were analyzed in the study. Both the adult rats (inoculated subcutaneously) and newborn rats (inoculated intradermally) were best fit by exponential model and both the distributions can be described by a single dose-response relationship. The BALB/C mice inoculated subcutaneously were best fit by Beta-Poisson models. The time post inoculation analysis showed that there was definite time and response relationship existed in this case.

Dose-Response Model for *Coxiella burnetii* (Q fever) (311,1019)

Things that are in progress LU 311

Author(s): Sushil Tamrakar

and Things that I have completed LU 1019

Author(s): Sushil Tamrakar

When Developing dose response model we wanted to develop dose-response model for Q fever

Experimental Design was as follows:

1- Mining the usable data, 2- Test for dose-response trend 3- Develop dose-response models 4- Evaluate best fit model 5- Low dose extrapolation.

Contribution:

exploring data

Results:

Data were explored and examined for the test of trend. Data were useful to further analyses.

Animal and Human Dose Response Models for *Brucella* species (1022,1023)

Things that are in progress LU 1022

Author(s): Sondra Teske

and Things that I have completed LU 1023

Author(s): Sondra Teske

When Developing environment we wanted to find out whether different data sets, and different routes of administration, or between subject species can be successfully pooled into defensible, comprehensive dose response model.

Experimental Design was as follows:

Exploring data, developing dose response models, pooling data, analyzing the results

Contribution:

Developing and pooling data sets developed a human dose response model for *Brucella melitensis*

Results:

Dose-response models were generated for prevalent species of *Brucella*: *Br. suis*, *Br. melitensis*, and *Br. abortus*. Dose-response models were created for aerosolized *Br. suis* exposure to guinea pigs from pooled studies. A parallel model for guinea pigs inoculated through both aerosol and subcutaneous routes with *Br. melitensis* showed that the median infectious dose corresponded to a 3.4 CFU (colony forming units) dose of *Br. suis*, much less than the N50 dose of about 100 CFU for *Br. melitensis* organisms. When *Br. melitensis* was tested subcutaneously on mice, the N50 dose was higher, 1,840 CFU. A dose response model was constructed from pooled data for mice, rhesus macaques and humans inoculated subcutaneously/ intradermally with *Br. melitensis*.

Human Outbreak analyses of *Brucella melitensis* (1024,1025)

Things that are in progress LU 1024

Author(s): Sondra Teske

and Things that I have completed LU 1025

Author(s): Sondra Teske

When Analyzing epidemiologic outbreak we wanted to find out whether the developed human dose response model can accurately be applied to analyzing outbreaks.

Experimental Design was as follows:

Using pooled animal and human time post inoculation-dose response model to analyze published data on human outbreaks to estimate initial dose exposure

Contribution:

The time post inoculation pooled animal human dose response model for *Brucella melitensis* could successfully be applied to approximating the initial exposure dosages in two separate outbreak incidences.

Results:

A pooled human-mouse-rhesus macaque dose-response model, and a human time post-inoculation (TPI) dose-response model were both used to estimate initial exposure dosages to two separate incidences of laboratory outbreaks of aerosolized *Brucella melitensis*. Workers in a vaccine manufacturing laboratory in Spain experienced a 17.1% overall attack rate to the exposure of *Br. melitensis* attributed to a failure of the air decontamination system. Estimates for exposure doses ranged from 98 CFU for the pooled animal-human dose response model and 343-1188 CFU for the human TPI model. A Michigan community hospital's microbiology lab was the site for the second laboratory outbreak caused by culturing of a vial outside of a biological safety hood. The attack rate of 31% was used to calculate an infectious dose of 5,263 CFU using the pooled animal-human dose response model, and a range of 179-354 CFU derived from the human TPI model.

Dissertation: Incorporating time to response into dose-response (445,1055)

Things that are in progress LU 445

Author(s): Yin Huang

and Things that I have completed LU 1055

Author(s): Yin Huang

When Developing dose response model we wanted to whether time-dose-response model could provide significantly acceptable fit to the human morbidity dose-response data and its modified form could be fitted with the response data of multiple-dose challenges in order to quantify the effect of different dosing schedules.

Experimental Design was as follows:

This is my dissertation work. The open literature will be searched for human time to response data and multiple challenges data. For available human morbidity dose-response data with the time to symptoms onset and the time to recovery, the initial appearance of symptoms will be chosen as the end point and the proposed time-dose-response model will be fitted with these human data using MLE method. For multiple challenge data, the probability of response caused by different dosing schedules will be compared by using more complex time-dose-response models.

Contribution:

The work presented is a component of a greater effort to develop human dose-response data for pathogenic organisms and present this information in the scientific literature and the general public. The project takes fundamental knowledge from a variety of disciplines, and uses quantitative methods of statistics and mathematical modeling to devise and verify a novel time-dose-response model, based on clinical, pathophysiological and epidemiological data. The resulting models advance our understanding on dose- and time-dependent probability distributions of disease risks, in vivo pathogenic kinetics after exposure to infectious agents, and the prediction of human epidemic curve based on animal experimental data.

Results:

This dissertation is the first instance that the time-dose-response models for MRA system are validated with data representing infections initiated by various pathogens. The classical exponential and beta-Poisson dose-response models were modified with dependencies of time post inoculation. These time

dependencies implicitly reflect the bacterial growth kinetics and quantify the time effect on dose response. The new models described the development of animal infectious response over time and represented observed responses accurately. The success of these models to fit survival data for disparate pathogens with very different characteristics indicates that the models are of an appropriate form and flexible enough to model the many processes occurring in diverse infections. The biological mechanism of the models can provide predictions of the in vivo pathogenic kinetics based on the host response. An example of this verification by a monkey inhalation tularemia model has been shown. An exciting finding in this current work is that the model predictions of inhalation anthrax incubation distribution based on animal data is significantly consistent with the human epidemic curve from the Sverdlovsk outbreak. The proposed models have been further modified to describe the multiple dosing challenges and quantify the effect of time intervals between individual challenges on the response.

Modeling the effect of multiple doses of scrapie agent (742,1055)

Things that are in progress LU 742

Author(s): Yin Huang

and Things that I have completed LU 1055

Author(s): Yin Huang

When Modeling dose response we wanted to find out if the modified form of the time-dose-response model could provide statistically acceptable fit to the response data of multiple-dose challenge of scrapie agent.

Experimental Design was as follows:

1) Collecting survival dose-response data of multiple challenge 2) Further developing the current time-dose-response models to describe the probability of response caused by different dosing schedules

Contribution:

The work presented is a component of a greater effort to develop human dose-response data for pathogenic organisms and present this information in the scientific literature and the general public. The project takes fundamental knowledge from a variety of disciplines, and uses quantitative methods of statistics and mathematical modeling to devise and verify a novel time-dose-response model, based on clinical, pathophysiological and epidemiological data. The resulting models advance our understanding on dose- and time-dependent probability distributions of disease risks, in vivo pathogenic kinetics after exposure to infectious agents, and the prediction of human epidemic curve based on animal experimental data.

Results:

This dissertation is the first instance that the time-dose-response models for MRA system are validated with data representing infections initiated by various pathogens. The classical exponential and beta-Poisson dose-response models were modified with dependencies of time post inoculation. These time dependencies implicitly reflect the bacterial growth kinetics and quantify the time effect on dose response. The new models described the development of animal infectious response over time and represented observed responses accurately. The success of these models to fit survival data for disparate pathogens with very different characteristics indicates that the models are of an appropriate form and flexible enough to model the many processes occurring in diverse infections. The biological mechanism of the models can provide predictions of the in vivo pathogenic kinetics based on the host response. An example of this verification by a monkey inhalation tularemia model has been shown. An exciting finding in this current work is that the model predictions of inhalation anthrax incubation distribution based on animal data is significantly consistent with the human epidemic curve from the Sverdlovsk outbreak. The proposed models have been further modified to describe the multiple dosing challenges and quantify the effect of time intervals between individual challenges on the response.

Comparison of animal-derived incubation with human outbreak data (1058,1055)

Things that are in progress LU 1058

Author(s): Yin Huang
and Things that I have completed LU 1055

Author(s): Yin Huang

When Validating dose response model we wanted to test if the animal-derived inhalation anthrax incubation distributions will be consistent with human epidemiological data from outbreaks

Experimental Design was as follows:

We will firstly collect the available time-to-response data of inhalation anthrax from animal studies and human outbreak. We will then review and expand a class of time-dose-response models to model theoretically the dose-dependent incubation time-to-response distribution. We will show the findings of the best-fit evaluation and parameter estimation for the candidate models fit to the animal data, and compare the predictions of low-dose incubation distribution based on the best-fit model with the outbreak data for verification.

Contribution:

The work presented is a component of a greater effort to develop human dose-response data for pathogenic organisms and present this information in the scientific literature and the general public. The project takes fundamental knowledge from a variety of disciplines, and uses quantitative methods of statistics and mathematical modeling to devise and verify a novel time-dose-response model, based on clinical, pathophysiological and epidemiological data. The resulting models advance our understanding on dose- and time-dependent probability distributions of disease risks, in vivo pathogenic kinetics after exposure to infectious agents, and the prediction of human epidemic curve based on animal experimental data.

Results:

This dissertation is the first instance that the time-dose-response models for MRA system are validated with data representing infections initiated by various pathogens. The classical exponential and beta-Poisson dose-response models were modified with dependencies of time post inoculation. These time dependencies implicitly reflect the bacterial growth kinetics and quantify the time effect on dose response. The new models described the development of animal infectious response over time and represented observed responses accurately. The success of these models to fit survival data for disparate pathogens with very different characteristics indicates that the models are of an appropriate form and flexible enough to model the many processes occurring in diverse infections. The biological mechanism of the models can provide predictions of the in vivo pathogenic kinetics based on the host response. An example of this verification by a monkey inhalation tularemia model has been shown. An exciting finding in this current work is that the model predictions of inhalation anthrax incubation distribution based on animal data is significantly consistent with the human epidemic curve from the Sverdlovsk outbreak. The proposed models have been further modified to describe the multiple dosing challenges and quantify the effect of time intervals between individual challenges on the response.

The relationship between bacterial kinetics and host response (1059,1055)

Things that are in progress LU 1059

Author(s): Yin Huang

and Things that I have completed LU 1055

Author(s): Yin Huang

When Validating dose response model we wanted to provide a direct verification of the biological validity of the time-dose-response models with in vivo pathogen growth.

Experimental Design was as follows:

Open literature will be searched for survival dose-response data and bacterial viable count data for monkeys infected by *F. tularensis* via inhalation route. The time-dose-response models by Huang et al. will be further developed to model quantitatively the hypothetical relationship between the host response and instantaneous microorganism number in vivo. The resulting models will be fit to survival dose-response data and the estimates of bacterial dynamics for different aerosol sizes were inferred. The

estimates will then be compared with the data of bacterial growth and the clinical and pathological findings for verification.

Contribution:

The work presented is a component of a greater effort to develop human dose-response data for pathogenic organisms and present this information in the scientific literature and the general public. The project takes fundamental knowledge from a variety of disciplines, and uses quantitative methods of statistics and mathematical modeling to devise and verify a novel time-dose-response model, based on clinical, pathophysiological and epidemiological data. The resulting models advance our understanding on dose- and time-dependent probability distributions of disease risks, in vivo pathogenic kinetics after exposure to infectious agents, and the prediction of human epidemic curve based on animal experimental data.

Results:

This dissertation is the first instance that the time-dose-response models for MRA system are validated with data representing infections initiated by various pathogens. The classical exponential and beta-Poisson dose-response models were modified with dependencies of time post inoculation. These time dependencies implicitly reflect the bacterial growth kinetics and quantify the time effect on dose response. The new models described the development of animal infectious response over time and represented observed responses accurately. The success of these models to fit survival data for disparate pathogens with very different characteristics indicates that the models are of an appropriate form and flexible enough to model the many processes occurring in diverse infections. The biological mechanism of the models can provide predictions of the in vivo pathogenic kinetics based on the host response. An example of this verification by a monkey inhalation tularemia model has been shown. An exciting finding in this current work is that the model predictions of inhalation anthrax incubation distribution based on animal data is significantly consistent with the human epidemic curve from the Sverdlovsk outbreak. The proposed models have been further modified to describe the multiple dosing challenges and quantify the effect of time intervals between individual challenges on the response.

3. Human Outbreak analyses of *Brucella melitensis* (1024,1022)

Things that are in progress unit Number 1024

Author(s): Sondra Teske

and Things that I have progress unit Number 1022

Author(s): Sondra Teske

Initially Analyzing epidemiologic outbreak we wanted to find out whether different data sets, and different routes of administration, or between subject species can be successfully pooled into defensible, comprehensive dose response model.

The original Experimental Design was as follows:

Whether different data sets, and different routes of administration, or between subject species can be successfully pooled into defensible, comprehensive dose response model.

We are currently trying to find out Whether the developed human dose response model can accurately be applied to analyzing outbreaks.

The current Experimental Design is as follows:

Using pooled animal and human time post inoculation-dose response model to analyze published data on human outbreaks to estimate initial dose exposure

4. Dose response for continuous oral exposure to *F. tularensis* (216,459)

Things that are in progress unit Number 459

Author(s): Carole Bolin

and Things that I have completed unit Number 216

Author(s): Carole Bolin

Once we learned:

A model of oral dose response to *F. tularensis* has been validated with additional data at

the low dose range strengthening the dose-response curve.

This result led us to the following research question: Determining dose response we wanted to find out if the dose response models differ if exposure to the agent is continuous over a period of days versus a bolus dose.

The current Experimental Design is as follows:

Mice will be exposed to continuous oral exposure to *F. tularensis* in drinking water and the dose response will be compared between mice receiving the same overall dose as a single oral bolus. Mice will be euthanized at various times post-exposure and quantitative cultures will be done on liver, spleen, and lungs. We will work with Dr. Rose to determine if *F. tularensis* adheres to different types of waterbottle materials prior to this experiment.

Dose response for repeated oral exposure to *F. tularensis* in mice (216,702)

Things that are in progress unit Number 702

Author(s): Carole Bolin

and Things that I have completed unit Number 216

Author(s): Carole Bolin

Once we learned:

A model of oral dose response to *F. tularensis* has been validated with additional data at the low dose range strengthening the dose-response curve.

This result led us to the following research question: Determining dose response we wanted to find out if the dose response parameters are different if the same total dose is given in a single bolus as opposed to repeated exposures over a series of hours or days. We hypothesize that the LD50 and ID50 will be reduced when the exposures are repeated over time.

The current Experimental Design is as follows:

Control mice will be exposed to one of four moderate to low doses of *Francisella* in a single bolus orally. Experimental groups will be given the same total dose of bacteria as the controls but administered in 5 doses administered over a period of 20 minutes, 10 hours, or 5 days. Mice will be euthanized at various times after exposure and quantitative culture of spleen, liver, and lung will be performed.

8. Outputs:

1. Students Supported:

Yin Huang PhD. Candidate, supervisor: Dr. Charles N. Haas

Sushil Tamrakar PhD. Candidate, supervisor: Dr. Charles N. Haas

2. Students Graduated:

Yin Huang PhD, supervisor: Dr. Charles N. Haas

3. Publications:

Yin Huang, Tao Hong, Timothy Bartrand, Patrick L. Gurian, Charles N. Haas, Ran Liu and Sushil Tamrakar "How Sensitive is Safe? Risk-based Targets for Ambient Monitoring of Pathogens," *IEEE Sensors Journal*, 10(3):668-673.

Sushil B. Tamrakar, Anne Haluska, Charles N. Haas, Timothy A. Bartrand. Dose-Response model for *Coxiella burnetii* (Q fever), in press, *Risk Analysis*

Quantification of the relationship between bacterial kinetics and host response for monkeys exposed to aerosolized *Francisella tularensis*

Manuscript titled "Quantification of the relationship between bacterial kinetics and host response for monkeys exposed to aerosolized *Francisella tularensis*", in press, *Applied and Environmental Microbiology*

4. Patents:
5. Presentations:
 - Dose-response model for *Coxiella burnetii*
 - Poster presentation in DHS students summit at Washington DC, 2010 by Sushil Tamrakar

Time-dose-response Model

Huang, Y. and Haas, C.N. Poster presented at the Society for Risk Analysis Annual Meeting, Baltimore, MD, December 6-9, 2009.

How Clean Is Clean? Risk Assessment for *Francisella tularensis* in Water

Huang, Y and Haas, C.N. PA Section AWWA 2010 Conference, Lancaster, PA, May 11 to 13, 2010.

6. Organization of workshops:
7. Participation in workshops:
8. Case studies algorithms developed:
9. Algorithms developed:
10. Human Resource Development:
11. Funds Leveraged (additional funding. resources for free):
12. Dissertation:
 - Dissertation titled: Incorporating Time to Response into Dose-Response Models Used in Quantitative Microbial Risk Assessment.
 - Yin Huang submitted his dissertation and completed his PhD degree in August 2010 under the supervision of Professor Charles Haas from Civil, Architectural & Environmental Engineering at Drexel University.

9. Outcomes:

Unit 459: Improve models to predict risk of environmental contamination with *F. tularensis*

Unit 702: Improve models to predict risk of environmental contamination with *F. tularensis*

Unit 729: dose-response model

Unit 1008: Dose-response model for *C. burnetii* is available and could be used by different units.

Unit 1009: In case of intentional or accidental released of aerosolized *R. rickettsii*, the dose-response model could be used to assess risk .

Unit 1017: Dose-response models for different hosts and different routes

Unit 1018: This estimation will be useful for the first responders and decision makers in case of accidental as well as intentional released of Rickettsial pathogens.

Unit 1019: dose-response model

Unit 1020: Create useable dose response model

Unit 1022: improve dose response models available

Unit 1023: Animal model can be applied to human model

Unit 1024: The time post inoculation pooled animal-human dose response model can be used to better estimate outbreak dosages

Unit 1025: This dose-response model can improve analysis of outbreaks

Unit 1027: Quantify and improve the dose response model available for *P. tularensis*

Unit 1055: The development of mechanistic time-dose-response models advances knowledge in microbial risk assessment, disaster preparedness, pathophysiological and epidemiological studies.

Unit 1058: The resulting animal models can be used to predict human response.

Unit 1059: The outcome on developing mechanistic models for tularemia may yield information on the mechanism by which the infection develops and potential strategies for controlling it

10. Integration with other projects:

An association was created between Unit 609, authored by Mark Weir (Project III, Drexel University) and Unit 469, authored by Patrick Gurian (Project IV, Drexel University)

An association was created between Unit 484, authored by Rachael Jones (Project I, U of California Berkeley) and Unit 481, authored by Shamia Hoque (Project III, Drexel University)

An association was created between Unit 481, authored by Shamia Hoque (Project III, Drexel University) and Unit 487, authored by Christopher Choi (Project I, U of Arizona)

An association was created between Unit 609, authored by Mark Weir (Project III, Drexel University) and Unit 530, authored by Patrick Gurian (Project IV, Drexel University)

An association was created between Unit 521, authored by Mark Weir (Project III, Drexel University) and Unit 540, authored by Jade Mitchell-Blackwood (Project IV, Drexel University)

An association was created between Unit 609, authored by Mark Weir (Project III, Drexel University) and Unit 540, authored by Jade Mitchell-Blackwood (Project IV, Drexel University)

An association was created between Unit 352, authored by Scott McLennan (Project V, Michigan State U) and Unit 669, authored by Mark Weir (Project III, Drexel University)

11. Anticipated Technical Results and Developments:

Project IV Report by Patrick P. Gurian

CAMRA Report for Year V (15 Sept 2009 – 14 Sept 2010) for Project IV

1. Project IV
2. Investigators: Patrick Gurian, Wandu Bruine de Bruin, Mitch Small, Julie Downs, Elizabeth Casman, Jade Mitchell-Blackwood, Tao Hong, Nicholas Ward, David Durham
3. Project Goals:
4. Tasks for Year V (15 Sept 2009 to 14 Sept 2010):

Dr. Elizabeth Casman’s Laboratory (Carnegie Melon University)

- 1.) Identify key issues from mental model interviews for follow up assessment with survey.
- 2.) Characterize understanding of flu, including limitations and gaps in knowledge
 - a. Preliminary analysis and internal CAMRA reports
 - b. Development of survey instruments
 - c. Testing and refinement of survey instrument
 - d. Recruitment of 200 subjects
 - e. Web survey
 - f. Analysis of survey results

Dr. Patrick Gurian’s Laboratory (Drexel University)

- 1.) Integration analysis of interview and survey results
- 2.) Internal CAMRA reports and peer reviewed publications
- 3.)

5. Research Activities

Researcher Name	Research Activity
Patrick L. Gurian	Supervise graduate student research Review and revise preliminary research products
Jade Mitchell Blackwood	Modeling dose response
Tao Hong	Modeling fate and transport
Kyle Griffith	Analyzing data from Idaho National Laboratories field test to estimate microbial recoveries obtained from different surfaces and sampling methods.
Heather Galada	Assisting dose response analysis Performing background research on existing response knowledge and gaps
Elizabeth Casman	Analyzing survey communicating Statement of Tasks

6. Background and prior research:

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. An Analysis of Microbial Spore Recovery Methods Things that are in progress LU (1031)

Author(s): Tao Hong

Experimental Design was as follows:

Potential health risks associated with biological agent surface contamination indoors have created a need for improved understanding of surface sampling in contamination assessment and resolution. In this paper, microbial spore recovery data from two separate large-scale (sample sizes are 1675 and 916 respectively) field dissemination experiments are examined to identify potential relationships between final spore concentrations and pre-defined parameters related to sampling methodology. The efficiency of various collection methods is analyzed for possible causality in microbial

spore recovery; while controlling for the effect of different test events, building rooms, object types, and surface types.

Finding Risk-Based Switchover Points for Response Things that are in progress LU (1039)

Author(s): Tao Hong

Experimental Design was as follows:

In the wake of the 2001 terrorist attacks, the use of *Bacillus anthracis* (anthrax) in bioterrorism attacks has emerged as a realistic concern. Thus, a contingency plan is needed in case of such an attack to inform decision makers about which response actions are appropriate and justified under which circumstances. This study considers the decisions: (1) to undertake prophylactic antibiotic treatment; (2) to vaccinate individuals prior to re-occupancy; or (3) to decontaminate the building in order to reduce risk for future occupants of a contaminated space. While these response actions are clearly justified for highly exposed individuals, a very large number of individuals exposed to very small risks in areas outside of the immediate vicinity of the release are also likely.

Statement of tasks for Project IV, Year VI Things that are in progress LU (1120)

Author(s): Elizabeth Casman

When communicating Statement of Tasks we wanted to find out how to perform those tasks

Experimental Design was as follows:

Complete papers on measuring flu risk perception: o Bruine de Bruin, W., Parker, A.M., & Maurer, J. (submitted). Measuring perceived invulnerability to H1N1 (swine) flu risks. *Journal of Risk and Uncertainty*. o Bruine de Bruin, W. & Carman, E.C. (in preparation). The effect of response format on reported risk perceptions. Target journal: *Journal of Risk and Uncertainty*. o Bruine de Bruin, W., Downs, J.S., & Casman, E. (in preparation). Decisions about flu prevention. Target journal: *Risk Analysis*.

2. Integrated Transport and Risk Model (422,1005)

Things that are in progress LU 422

Author(s): Tao Hong

and Things that I have completed LU 1005

Author(s): Tao Hong

When Modeling fate and transport we wanted to find out the distribution of *Bacillus anthracis* in an office suite after releasing

Experimental Design was as follows:

Model is built based on a simple office suite with a heating ventilation and air conditioning (HVAC) system. We divide the office into 7 internal compartments: air, tracked floor, untracked floor, walls, ceiling, HVAC, and the nasal passages of an occupant of the office. In order to obtain mass-balance closure, we add another compartment to the system consisting of all areas external to the room. We obtain the following system of linear first order ordinary differential equations based on using the mass balance relationships among different compartments in the office suite. We obtain the following system of linear first order ordinary differential equations based on using the mass balance relationships among different compartments in the office suite.

Contribution:

This paper synthesizes available information on five Category A pathogens (*B.anthraxis*, *Y.Pestis*, *F. tularensis*, *Variola major* and *Lassa*) to develop quantitative guidelines for how environmental pathogen concentrations may be related to the human health risk.

Results:

An integrated model of environmental transport and human health exposure to biological pathogens is constructed which 1) including the effects of environmental attenuation, and 2) considering contact exposure (dermal and ingestion risk) as well as

inhalational exposure. A new metric designed to evaluate different pathogens' threats is derived. In this study, two scenarios are considered 1) retrospective scenario, to link environmental concentrations of pathogens with the risks experienced by previous occupants of the building after an aerosol release of pathogens; and 2) prospective scenario, to link environmental concentrations on surfaces to the risks which future occupants would experience if the building is re-occupied. Monte Carlo methods are used to assess uncertainty in the results and identify important uncertainties in input parameters so that future research may be directed towards reducing these uncertainties.

Integrated Transport and Risk Model (422,1006)

Things that are in progress LU 422

Author(s): Tao Hong

and Things that I have completed LU 1006

Author(s): Tao Hong

When Modeling fate and transport we wanted to find out the distribution of *Bacillus anthracis* in an office suite after releasing

Experimental Design was as follows:

Model is built based on a simple office suite with a heating ventilation and air conditioning (HVAC) system. We divide the office into 7 internal compartments: air, tracked floor, untracked floor, walls, ceiling, HVAC, and the nasal passages of an occupant of the office. In order to obtain mass-balance closure, we add another compartment to the system consisting of all areas external to the room. We obtain the following system of linear first order ordinary differential equations based on using the mass balance relationships among different compartments in the office suite. We obtain the following system of linear first order ordinary differential equations based on using the mass balance relationships among different compartments in the office suite.

Results:

The results indicate that Hong's fate and transport model overestimates released spores' settling velocity, while the resuspension process for the released spores has been underestimated. Also, the posterior size distributions of released pathogens refer that more larger particles were released in the 2001 attack, and it is estimated about 15% of pathogens left the room where they are released. This BMC application updated the parameter ranges in a complex indoor air fate and transport model and provided new insights on parameters' inputs and outputs.

Finding Risk-Based Switchover Points for Response (1039,1041)

Things that are in progress LU 1039

Author(s): Tao Hong

and Things that I have completed LU 1041

Author(s): Tao Hong

Experimental Design was as follows:

In the wake of the 2001 terrorist attacks, the use of *Bacillus anthracis* (anthrax) in bioterrorism attacks has emerged as a realistic concern. Thus, a contingency plan is needed in case of such an attack to inform decision makers about which response actions are appropriate and justified under which circumstances. This study considers the decisions: (1) to undertake prophylactic antibiotic treatment; (2) to vaccinate individuals prior to re-occupancy; or (3) to decontaminate the building in order to reduce risk for future occupants of a contaminated space. While these response actions are clearly justified for highly exposed individuals, a very large number of individuals exposed to very small risks in areas outside of the immediate vicinity of the release are also likely.

Results:

Our results indicate that there are non-negligible risk thresholds below which response actions produce more costs than benefits. For the base case, the thresholds range from a risk of 1 in 33 for

environmental decontamination by fumigation to 1 in 6,547 for antibiotic prophylaxis and 1 in 7,108 for vaccination. A one-way sensitivity analysis on uncertain variables indicate less than an order of magnitude change in these thresholds. Benefit-cost analysis is a useful tool for assessing trade-offs among alternative decision responses, but it has some limitations as well. Analyses such as this cannot be the sole criterion in responding to bioterrorism incidents.

8. Outputs:

1. Students Supported:

Primary support from CAMRA:

Tao Hong, doctoral student, supervisor: Dr. Patrick Gurian

Students contributing to CAMRA but with the majority of support from outside CAMRA:

Ian Solon, M.S. student, supervisor: Dr. Patrick Gurian

Kyle Griffith, M.S. student, supervisor: Dr. Patrick Gurian

Heather Galada, MPH student, supervisor: Dr. Patrick Gurian

Jade Mitchell-Blackwood, doctoral student, supervisor: Dr. Patrick Gurian

2. Students Graduated:

Jade Mitchell-Blackwood received her doctoral degree in the summer of 2010.

Ian Solon received his M.S. and finished a Master thesis entitled "The extraction of a *B. anthracis* Surrogate from Pleated HVAC Filters" in the Spring of 2010.

3. Publications:

Hong, T., P. L. Gurian, and Nicolas Ward "Setting Risk-Informed Environmental Standards for *Bacillus Anthracis* Spores," *Risk Analysis* 30(10): 1602-1622.

Mitchell-Blackwood, J., P.L. Gurian, C. O'Donnell. "Finding Risk-based Switchover Points for Response Decisions for Environmental Exposure to *Bacillus anthracis*" submitted to *Human and Ecological Risk Assessment* (in press).

Yin Huang, Tao Hong, Timothy Bartrand, Patrick L. Gurian, Charles N. Haas, Ran Liu and Sushil Tamrakar "How Sensitive is Safe? Risk-based Targets for Ambient Monitoring of Pathogens," *IEEE Sensors Journal*, 10(3):668-673.

Bruine de Bruin, W., Parker, A.M., & Maurer, J. (submitted). Measuring perceived invulnerability to H1N1 (swine) flu risks. *Journal of Risk and Uncertainty*.

4. Patents:

5. Presentations:

Identifiability of Bioaerosol Transport and Risk Models by Environmental Sampling
Hong T, Gurian P, presented in Risk Analysis Annual Meeting 2009

Presentation on Measuring perceived invulnerability to H1N1 (swine) flu risks

Bruine de Bruin, W., Parker, A.M., & Maurer, J. (2010). Measuring perceived invulnerability to H1N1 (swine) flu risks. Invited presentation at the Workshop on Internet Interviewing about Health and Retirement, Munich Germany.

6. Organization of workshops:

7. Participation in workshops:

Participation in Workshop on Internet Interviewing about Health and Retirement
Workshop on Internet Interviewing about Health and Retirement, University of

Munich, Munich, Germany. March 22, 2010.
Accomplishments byWandi Bruine de Bruin

Participation in Workshop on the Health and Retirement Internet Study
Workshop on the Health and Retirement Internet Study, University of Michigan, Ann Arbor, MI.
October 12, 2010.

Accomplishments byWandi Bruine de Bruin

8. Case studies algorithms developed:
9. Algorithms developed:
10. Human Resource Development:
11. Funds Leveraged (additional funding. resources for free):
12. External collaboration:

Collaboration the University of Tilburg

We are collaborating with Katherine Carman at the University of Tilburg on a national survey on flu risk perceptions with a national sample recruited through the Longitudinal Internet Study for the Social Sciences.

Accomplishments byWandi Bruine de Bruin

Collaboration with the Pittsburgh office of the RAND Corporation

We are collaborating with Andrew Parker at the Pittsburgh office of the RAND Corporation, and with J. Maurer Washington office of the RAND Corporation, conducting an ongoing survey about H1N1 risk perceptions with a national sample recruited through the American Life Panel.

Accomplishments byWandi Bruine de Bruin

9. Outcomes:

Unit 1005: Results indicate that in the retrospective scenario, risk from inhalation is the main component of the overall risk, while risk from ingestion (dermal contact for B. anthracis) is the main component of the overall risk in the prospective scenario. Pathogens' threats in an air release is dominated by their virulence, while the pathogen fomite decay rates control the threats in a surface release.

Unit 1031: A review of the results reveals that the collection method and location with respect to release source have a statistically significant relationship with microbial recovery rates. Across both data sets, the wipe collection method produces the highest mean spore recovery compared to that of the swab, and sock vacuum, indicating its potential effectiveness to sample contaminated surfaces.

Unit 1039: Our results indicate that there are non-negligible risk thresholds below which response actions produce more costs than benefits. For the base case, the thresholds range from a risk of 1 in 33 for environmental decontamination by fumigation to 1 in 6,547 for antibiotic prophylaxis and 1 in 7,108 for vaccination. A one-way sensitivity analysis on uncertain variables indicate less than an order of magnitude change in these thresholds. Benefit-cost analysis is a useful tool for assessing trade-offs among alternative decision responses, but it has some limitations as well. Analyses such as this cannot be the sole criterion in responding to bioterrorism incidents.

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

An association was created between Unit 207, authored by Elizabeth Casman (Project IV, Carnegie Mellon) and Unit 424, authored by Scott McLennan (Project IV, Michigan State U)

An association was created between Unit 372, authored by Sheng Li (Project II, U of Michigan) and Unit 426, authored by Scott McLennan (Project IV, Michigan State U)

An association was created between Unit 609, authored by Mark Weir (Project III, Drexel University)

and Unit 469, authored by Patrick Gurian (Project IV, Drexel University)

An association was created between Unit 469, authored by Patrick Gurian (Project IV, Drexel University) and Unit 478, authored by Mark Nicas (Project I, U of California Berkeley)

An association was created between Unit 609, authored by Mark Weir (Project III, Drexel University) and Unit 530, authored by Patrick Gurian (Project IV, Drexel University)

An association was created between Unit 609, authored by Mark Weir (Project III, Drexel University) and Unit 540, authored by Jade Mitchell-Blackwood (Project IV, Drexel University)

An association was created between Unit 521, authored by Mark Weir (Project III, Drexel University) and Unit 540, authored by Jade Mitchell-Blackwood (Project IV, Drexel University)

An association was created between Unit 748, authored by Ian Spicknall (Project II, U of Michigan) and Unit 762, authored by Patrick Gurian (Project IV, Drexel University)

11. Anticipated Technical Results and Developments:

Project V Report by Rosina Weber

CAMRA Report for Year V (Sep 15 2009 to Sep 14 2010) for Project V

1. Project V
2. Investigators: Yuan An, Rosina Weber, Sidath Gunawardena
3. Project Goals:
4. Tasks for Year V (15 Sept 2009 to 14 Sept 2010):

Dr. Rosina Weber's Laboratory (Drexel University)

- 1.) Design and implement MicrobialRisk.net Wiki
- 2.) Approve final version and move CAMRA Knowledge Repository to CAMRA designated server.

5. Research Activities

Researcher Name	Research Activity
Rosina Weber	communicating Statement of Tasks
Sidath Gunawardena	Investigating Collaborators Investigating Collaboration

6. Background and prior research:

7. Research Contributions this Year:

1. Successful Multidisciplinary Collaboration in Academia Things that are in progress LU (1113)

Author(s): Sidath Gunawardena

When Investigating Collaborators we wanted to find out factors that contribute to the success of multidisciplinary collaboration

Experimental Design was as follows:

Examine the literature on collaboration in the fields of information science,

organizational behavior, education, computer supported collaborative work, public policy management, and sociology

Statement of Tasks for Year VI for Project V Things that are in progress LU (1161)

Author(s): Rosina Weber

Experimental Design was as follows:

Collaborate on a manuscript on QMRA knowledge and information WIKI 1. Transfer wiki hosting to MSU servers 2. Assessment to determine how to conduct the building of the semantic wiki 3. Create concepts for semantic wiki KR 1. Creating documentation of new KR features in a user guide 2. Creating documentation for server maintenance and recovery 3. Fix existing bugs, design improvements, and maintain CAMRA KR

2. Successful Multidisciplinary Collaboration in Academia (1113,1114)

Things that are in progress LU 1113

Author(s): Sidath Gunawardena

and Things that I have completed LU 1114

Author(s): Sidath Gunawardena

When Investigating Collaborators we wanted to find out factors that contribute to the success of multidisciplinary collaboration

Experimental Design was as follows:

Examine the literature on collaboration in the fields of information science, organizational behavior, education, computer supported collaborative work, public policy management, and sociology

Contribution:

Success in multidisciplinary collaboration can be facilitated by: 1. Including researchers who have a diverse disciplinary background as they are more likely to be open to the different research paradigms encountered 2. Such researchers are also more likely to act as bridges within the collaboration, facilitating communication and the building of trust 3. Including senior faculty who can act as mediators and manage conflict

Results:

The literature in the fields of information science, organizational behavior, education, computer supported collaborative work, public policy management, and sociology do not share a consistent definition of collaboration. Multidisciplinary collaboration is an emerging focus of study.

8. Outputs:

1. Students Supported:

Sidath Gunawardena

2. Students Graduated:

3. Publications:

Gunawardena, S., Weber, R., & Agosto, D. E. (2010). Finding that Special Someone: Modeling Collaboration in an Academic Context. *Journal of Education in Library and Information Science* 51(4)

4. Patents:

5. Presentations:

Gunawardena, S., Weber, R., & Agosto, D. E. (2010). Finding that Special Someone: Modeling Collaboration in an Academic Context. Presented at Creating a Culture of Collaboration, 2010 ALISE Annual Conference, Boston MA, January 12-15.

6. Organization of workshops:
7. Participation in workshops:
8. Case studies algorithms developed:
9. Algorithms developed:
10. Human Resource Development:
11. Funds Leveraged (additional funding. resources for free):
Modeling Collaboration in an Academic Context
Best paper award for Gunawardena, S., Weber, R., & Agosto, D. E. (2010). Finding that Special Someone: Modeling Collaboration in an Academic Context. Presented at Creating a Culture of Collaboration, Journal of Education in Library and Information Science 51(4)

9. Outcomes:

10. Integration with other projects (association between units in different projects): An association was created between Unit 352, authored by Scott McLennan (Project V, Michigan State U) and Unit 669, authored by Mark Weir (Project III, Drexel University)
An association was created between Unit 58, authored by Rosina Weber (Project V, Drexel University) and Unit 877, authored by Christopher Choi (Project I, U of Arizona)

11. Anticipated Technical Results and Developments:

Appendix C: Statement of Tasks for Year 5

Project	Laboratory	Task and Brief Description
I	Mark Nicas UC Berkeley	3.) Influenza RNA viruses in hospitals during the 2010/2011 winter flu season at Moffitt Hospital. Testing with qPCR of; air, surfaces and protective equipment of nurses attending Influenza A and B patients. 4.) Human study in 2010/2011 winter flu season to provide direct estimate of number of viruses to be delivered to facial target sites via droplet spray pathway.
	Christopher Choi UAZ	3.) Effects of the axial dispersion coefficients in water distribution systems and updated AZRED (improved adaptation of EPANET) 4.) Event based microbial risk assessment and response analysis of <i>Cryptosporidium</i> in potable water distribution systems
	Charles P. Gerba UAZ	5.) Complete collection of data on the transfer and survival of non-pathogenic surrogates (MS-2 coliphage, <i>Escherichia coli</i> , a gram positive bacterium, <i>Bacillus</i> spp. spores). Will be used to assess the transfer from contaminated hands to fomites and from contaminated fomites to hands. 6.) Since bacteria which possess a lipid membrane may have different transfer rates survival and transfer experiments will also be conducted with vaccine influenza virus. 7.) Data gathered in objectives 1 and 2 will be analyzed relative to the various study factors and placed in a spread sheet to be usable by groups II and IV in risk model assessment. 8.) Assessment of human collagen artificial skin for use in transfer experiments involving bio-threat agents. 9.) A literature review will also be conducted on previous work on the transfer of microorganisms from skin to fomites and fomites to hands, as well as survival on the skin.
II	Joe Eisenberg & Jim Koopman Univ MI	4.) Continue development of the Environmental Infection and Transmission System (EITS) models. Main focus during Year 5 will be to examine the impact of behavior and movement patterns on the transmission of Influenza and ultimately on risk. 5.) Finalize dose timing dose response model analysis, using multiple dosing data from an Anthrax observational study with monkeys. 6.) Application of EITS for: <ul style="list-style-type: none"> a. Examining the impact of realistic interventions (hand hygiene, masks, decontamination, and cough etiquette) on minimizing risk.

		<ul style="list-style-type: none"> b. Examining the impact of social structure on the indirect risks associated with outbreaks. c. Examining the risk of MSRA in hospital settings, developing of a detailed realistic EITS model for the surgical intensive care unit (SICU) at the University of Michigan hospital, and examining the effects of cleaning and decontamination in the SICU. d. Examining the impact of decontamination of desktops in schools on minimizing absenteeism.
III	Charles N. Haas Drexel	<p>Administrative:</p> <ul style="list-style-type: none"> 4.) Assist director with overall management tasks and scientific leadership. 5.) Work with director to interface with US EPA, DHS and other external constituents. 6.) Assist director with coordination of cross-project activities. <p>Modeling:</p> <ul style="list-style-type: none"> 16.) Mechanistic model of multiple exposure routes and interspecies relationships 17.) Mechanistic incorporation of time post inoculation for <i>Bacillus anthracis</i> (<i>B. anthracis</i>), <i>Francisella tularensis</i> (<i>F. tularensis</i>) and <i>Yersinia pestis</i> (<i>Y. pestis</i>). 18.) Collaboration with Project II on coupling of dose response time models to population models. 19.) Modeling multiple dosing <i>F. tularensis</i> data when made available from Michigan State University (MSU). 20.) Kinetics modeling of multiple dosing data when made available from MSU. 21.) Verification of mechanistic basis of time-dose response model, demonstrating use to predict <i>in-vivo</i> bacterial kinetics based on host response will be finalized. 22.) A paper that estimates the dose-dependent incubation distribution of inhalation anthrax based on animal data and shows a consistency of the prediction for low-dose response with human data from Sverdlovsk outbreak will be finalized. 23.) Time to response for avian influenza A (H5N1) infection. 24.) Study infectious effect on hamsters exposed repeatedly to scrapie agent. 25.) In collaborative work with Project IV, combining dose-response analysis and stochastic human exposure models, for estimating the impact of human behaviors and transfer coefficients on the probability of infection caused by an intentional release of <i>Norovirus</i>. 26.) Collaboration with Project IV to integrate the time-dose-response model with an ordinary differential equation system that predicts the fate and transport of various Category A biological agents, in order to estimate the infection dynamics of a population exposed to those

		<p>agents in an indoor environment.</p> <p>27.) Multiple routes exposure and interspecies relationships of <i>Rickettsial</i> diseases such as Rocky Mountain spotted fever and murine typhus.</p> <p>28.) Mechanistic dose response model will be developed for <i>Brucella</i> species (including <i>B. melitensis</i>, <i>B. suis</i>, and <i>B. abortus</i>)</p> <p>29.) Post exposure time dependence of dose response for <i>Brucella</i> will be completed, with cross-comparisons to outbreak data.</p> <p>30.) Continuing the work on outbreak data validations for different pathogens.</p>
IV	<p>Elizabeth Casman Carnegie Mellon</p> <p>and</p> <p>Patrick L. Gurian Drexel</p>	<p>1.) Identify key issues from mental models interviews for follow-up assessment with survey.</p> <p>2.) Characterize understanding of flu, including limitations and gaps in knowledge.</p> <ol style="list-style-type: none"> a. Preliminary analysis and internal CAMRA reports. b. Development of survey instrument. c. Testing and refinement of survey instrument. d. Recruitment of 200 subjects. e. Web survey. f. Analysis of survey results. <p>3.) Integrated analysis of interview and survey results.</p> <p>4.) Internal CAMRA reports and peer-reviewed publication.</p>
V	Rosina Weber Drexel	<p>3.) Design and implement MicrobialRisk.net Wiki</p> <p>4.) Approve final version and move CAMRA Knowledge Repository to CAMRA designated server.</p>

Appendix D: CAMRA Expenditures

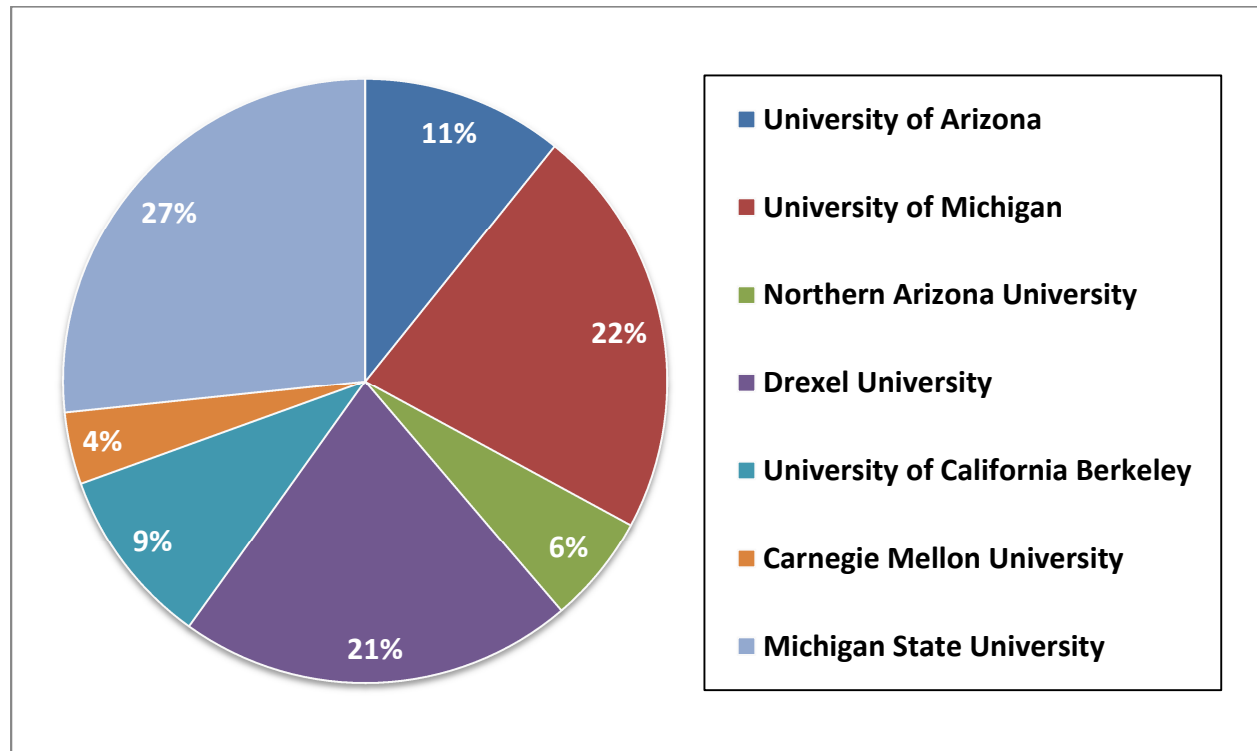
Remaining budget for Dec. 2010 to March 2012 for the last 16 months of the Center is \$3,2 million.

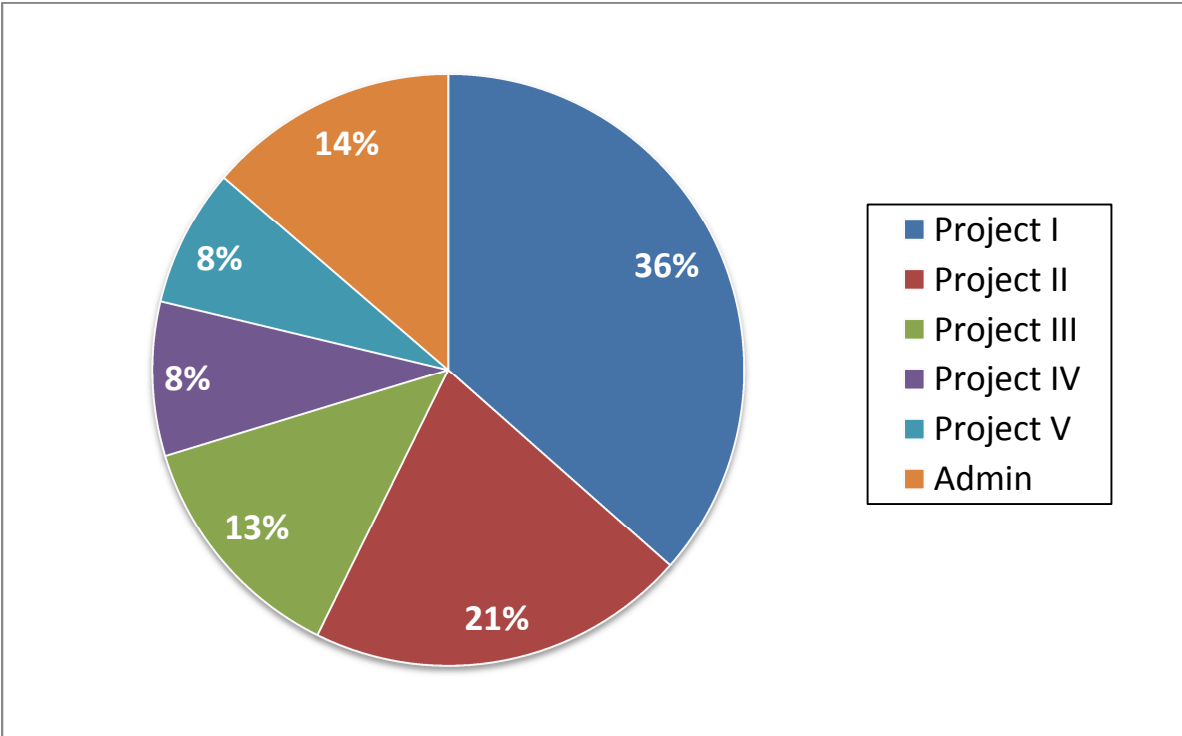
(Budget is allocated for the animal studies which were delayed due to Dr. Bolin’s illness and for the development of the Microbial Risk WIKI as well as the budgets for each university).

Funds for final audits and site visits are allocated for 2011.

Funds for ALL PI meeting are set aside for March 2011.

University	With Pending Total Spent	Percent Total
University of Arizona	\$730,206.79	0.11
University of Michigan	\$1,494,091.10	0.22
Northern Arizona University	\$395,521.79	0.06
Drexel University	\$1,431,545.43	0.21
University of California Berkeley	\$648,913.29	0.10
Carnegie Mellon University	\$259,482.27	0.04
Michigan State University	\$1,802,864.64	0.27
Total	\$6,762,625.31	





PI	School
Project I	
Dr. Charles P. Gerba	University of Arizona
Dr. Christopher Choi	
Dr. Mark Nicas	University of California Berkeley
Dr. Syed Hashsham	Michigan State University
Dr. David Wagner	Northern Arizona University
Project II	
Dr. James Koopman	University of Michigan
Dr. Joseph Eisenberg	
Project III	
Dr. Charles N. Haas	Drexel University
Dr. Carol Bolin	Michigan State University
Project IV	
Dr. Patrick L. Gurian	Drexel University
Elizabeth Casman	Carnegie Mellon University
Project V	
Dr. Rosina Weber	Drexel University
Administration	
Dr. Joan B. Rose	Michigan State University
Dr. Charles N. Haas	Drexel University

Appendix E: QA Report by Rebecca Ives



QUALITY ASSURANCE REPORT

**Center for Advancing Microbial Risk Assessment
Year-5**

Submitted by: Ms. Rebecca Ives
Quality Assurance Officer
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13 Natural Resources
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ivesrebe@msu.edu

Submitted to
Dr. Irwin Baumel
U.S. Environmental Protection Agency (EPA)

And
Dr. Matthew Clark
Department of Homeland Security (DHS)
Washington DC
November 22, 2010 report

Quality Management Plan (QMP):

The annual review of the QMP was completed in November 2010. Minor revisions of Dr. Eisenberg's responsibilities were made to reflect his responsibilities as Quality Assurance Manager for the MRSA component of Project 2

According to the Quality Management Plan of the Center for Advancing Microbial Risk Assessment (CAMRA), each of the projects was to develop and implement a quality assurance project plan (QAPP) addressing the major elements contained in EPA guidance document, EPA QA/G-5 "Guidance for Quality Assurance Project Plans." With the exception of projects 2 and 5, the projects are subdivided by task among principal investigators. As a result, all projects except project 2 and 5 have multiple QAPPs covering the responsibilities and research objectives under the management of the principal investigator. The QAPPs have been given a numerical designation for organizational purposes. Each principal investigator is either the quality assurance manager for that location/task, or has designated personnel to act in that capacity.

QAPP P2Q6 was delayed due to health problems of the project Quality Assurance Manager, Dr Koopman. With the exception of P2Q6, all final QAPPs were approved by the CAMRA Directors and the Quality Assurance Officer, Rebecca Ives.

TABLE A

Project	QAPP #	PI	University	Current QAPP Title & Version	Date QAPP Submitted to QAO	Comments made by QAO* and returned to PI	Date QAPP Approved by QAO	Date approved by CAMRA directors
I	1	Chuck Gerba	AZ	QAPP P1Q1 Gerba v5_0.doc	10/10/2010	10/12/10	10/12/10	
I	2	Chris Choi	AZ	QAPP P1Q2 Choi v5_0.doc	9/23/2010	9/23/2010	9/23/2010	10/26/10
I	3	Syed Hashsham	MSU	QAPP P1Q3 Hashsham v3_0.doc	8/15/2010	8/19/2010	8/19/2010	10/8/10
I	4	Mark Nicas	UCBerkeley	QAPP P1Q4 Nicas v5_0.doc	3/10/2010	11/22/2010	11/22/2010	
I	5	David Wagner	NAU	QAPP P1Q5 Wagner v5_0.doc	08/12/10	10/04/10	10/06/10	10/8/10
II	6	Jim Koopman	UM	QAPP P2Q6 Koopmanv5_0.doc	Delayed due to health problems of project Quality Assurance Manager			
III	7	Chuck Haas	Drexel	QAPP P3Q7 Haas v5_0.doc	8/10/2010	8/19/2010	8/23/2010	10/8/10
III	8	Carole Bolin	MSU	QAPP P3Q8 Bolin v5_0.doc	No change, carryover of approval from year 4			
IV	9	Patrick Gurian	Drexel	QAPP P4Q9 Gurian v5_0.doc	11/17/2010	11/19/2010	11/19/2010	
IV	10	Liz Casman	CMU	QAPP P4Q10 Casman v5_0.doc	8/13/2010	8/19/2010	8/26/2010	10/26/10
V	11	Rosina Weber	Drexel	QAPP P5Q11 Weber v5_0.doc	11/9/2010	11/12/2010	11/15/2010	

* Date of last set of comments made by the QAO.

Audits

All audits for year 5 are pending. All audits for year 5 will be site visits and will be scheduled to coincide with meetings between project personnel and LeiLei Qian, who is responsible for the CAMRA MicroRisk Wiki project. The start date of LeiLei Qian is December 15. An update to the quality assurance report will be submitted once all audits are completed.