Quantification of the Effects of Age on the Dose Response of *Variola major* in Suckling Mice

Mark H. Weir, Charles N. Haas
Drexel University, Civil Architectural and Environmental Engineering Department/Center for Advancing Microbial Risk Assessment

Project Scope:
The work presented in this poster is a component of a greater effort to develop human dose response data for pathogenic organisms and present this information to the scientific community and general public. Dose response data in the technical literature are generally the results of animal experimental studies or from epidemiological studies. Therefore, a significant thrust of this project is the use of fragmentary data to develop estimates of microbial risk for human populations. Data have been collected for all Category A bioterror agents, most Category B agents and other agents of concern such as *Vibrio cholera* and *Mycobacterium tuberculosis*. Future work will focus on incorporation of microbial kinetics, epidemiological data and other techniques for developing dose response models for pathogens with limited or no experimental dose response data.

Recent Progress:
Dose response data for *Variola major* (*V. major*), the causative agent of smallpox, were obtained from open literature, summarized and fitted with the exponential, beta Poisson and log Probit dose response models. It is known from prior outbreak experience that there is generally a difference in the infectivity of the agent as well as mortality based on age of the patient. A source of animal dose response data was found with age delineation for the exposure group (suckling mice intraperitoneal exposure). This delineation was used to fit dose response models which incorporated age dependency. The fits were obtained using maximum likelihood estimation (MLE). The effect of host age dependency could be quantitatively described using modifications of the beta Poisson and exponential dose response models.

Future Plans:
Future work will include further dose response modeling of *V. major* and if these data are also age delineated, validation of these modified models will be performed. Beyond this work on *V. major*, further work in the project will include development of mechanistic and advanced dose response models.

Relevance to Listed Research Areas:
This work contributes to the Department of Homeland Security's biological threats and countermeasures research needs by quantifying the effect age has on the dose response models for *V. major* in suckling mice. This effect is known in a clinical sense that different age groups are affected in varying degrees of severity by *V. major*. This work quantitatively includes this known difference into the dose response models. Results can contribute to improved safety for first responders and medical personnel in response to bioterror attacks.