

Understanding “Dose” in an Aerosol Animal Model:
 $D = C \times MV \times t_{exp}$

0900 – 0915

Welcome/Housekeeping/Introduction

0915 - 0945

Dose Calculations: Consider the Differences and Similarities between Scientific Fields

Elizabeth K. Leffel, PhD, M.P.H.

National Biodefense Analysis and Countermeasures Center

The objective of this workshop introduction is to present the subject matter to be discussed throughout the course. The variables of the dose equation ($D = C \times MV \times t_{exp}$) will be introduced, with examples of how each variable has an impact on the final calculation. The importance of study designs, planning, and recognition of challenges will be highlighted. Later talks will address considerations used in either pharmaceutical, environmental, or infectious disease studies. At the conclusion of this section, participants will understand that calculating a presented dose may be defined differently, depending on what question is answered.

0945 - 1020

Defining Aerosol Dose in the Pharmaceutical and Environmental Space: Practical Impacts on Risk Assessment and Treatment Paradigms in Animals and Man

Matthew D. Reed, PhD, DABT

Lovelace Respiratory Research Institute

This presentation will focus on the methodologies used to calculate the inhaled dose of aerosols by empirical and calculated means in tidal breathing and "forced maneuver" paradigms. Tidal breathing is consistent with environmental exposure (e.g., air pollution) and clinical (nebulizer) drug treatments. "Forced maneuvers" utilize the patients forced inspiratory ventilation (FIV) or mechanical/ compressed gas and FIV to delivery medications (e.g., dry powder inhaler or metered dose inhaler respectively). Differences among species in the airway size and ultrastructure as well as particle size have an impact on final determination of animal/ human "inhaled deposited dose" within the respiratory tract. These factors impact subsequent risk assessment (environmental and preclinical toxicology) and treatment paradigms in normal and diseased animal models and patient populations. An understanding of these concepts will benefit those individuals designing experiments utilizing 1) inhaled bio and chemical threat animals models and 2) inhaled treatment paradigms for bio and chemical threat agents.

1020 – 1035 BREAK

1035 – 1110

Experimental Dose in Infectious Disease Studies: Accounting for Depositional Fraction

Chad J. Roy, Ph.D., M.S.P.H.

Tulane University School of Medicine/Tulane National Primate Research Center

Estimation of experimental aerosol dose in infectious disease studies involving high consequence pathogens is an essential component to better understanding host response as it relates to disease pathogenesis or predicted response when evaluating medical products. Methodology for accurately and reliably approximating experimental dose hinges upon defining a constellation of physical and biological factors. In this presentation, input variables important to dose estimation will be identified and reviewed. Prevailing methods used to further dissect dose in the context of studies involving infectious bioaerosols will be presented. Special emphasis will be placed on the impact of depositional fraction from multimodal aerosol exposure upon experimental dose, using both historical and recently published data sources. Benefits from this presentation will include an appreciation of the prevailing methods that can be used to integrate fractional deposition into experimental dose estimation in infectious disease studies.

1110 - 1145

Pulmonary Drug Delivery in an Infectious Disease Animal Model

Lucila Garcia-Contreras, Ph.D.

School of Pharmacy, University of North Carolina at Chapel Hill

The objective of this presentation is to review the ways in which a drug or vaccine dose may be defined and interpreted in pulmonary delivery studies employing healthy and infected animal models, and the influence of dose in the outcome of efficacy studies. Two major diseases will be reviewed that affect lung morphology and function, namely cystic fibrosis and tuberculosis. The relevant animal models for each disease and their suitability in extrapolating the results of pharmacokinetic and pharmacodynamic studies to humans will be discussed. Different types of doses used in pulmonary delivery studies will be presented with methods of administration commonly employed in these studies. The importance of accurately determining the dose delivered and the impact that this will have on the design of pharmacokinetic studies will be illustrated with some examples. Lastly, the impact of considering and controlling the variables in the success of treatment will be presented as an example of a study employing the guinea pig model of tuberculosis.

1145 -1200

Panel: Questions submitted during break and then addressed in sequence