



ISAM 2011 Conference abstract

Title: DEPOSITION OF AEROSOLIZED LIQUID FORMULATION IN FERRETS BY 3D CT/SPECT IMAGING

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PURPOSE: While the ferret model is a gold standard pre-clinical model for the evaluation of Influenza therapies, to date no quantitative aerosol deposition data has been reported in the model.

METHOD: The deposition pattern of an aerosolized radio-labeled liquid formulation was quantified using 3D CT-SPECT for 4 ferrets after aerosol exposure in a rodent inhalation exposure system. A dilute aqueous solution of calcium chloride and sodium chloride was labeled with sulfur colloid and Tc^{99m} and nebulized with a Pari LC nebulizer. The label integrity was validated at the exposure ports. The delivered aerosol had an MMAD=2.8 μ m and GSD=1.8. Aerosol exposure was performed for each ferret independently followed immediately by anesthetization and imaging. Exposed doses were calculated from the exposure time (5 min), measured body weight (BW; kg), respiratory minute volume (RMV = 0.499xBW^{0.809} from Bide et al. 2000), and measured radioactivity concentration (mCi/L).

RESULTS: Total measured radioactivity deposited in the ferret respiratory tract was 34 \pm 8% of the exposed dose (mean \pm SE). Regional deposited fractions of the exposed dose were: Lung 7.6 \pm 2.1%, Nasal 9.5 \pm 5.1%, Oropharynx 10.9 \pm 2.7%, and Laryngopharynx 5.9 \pm 1.8%.

CONCLUSIONS: Respiratory tract aerosol delivery was demonstrated to be feasible in ferrets. Measured values of both the total and regional deposition may allow for dose prediction in ferrets for similarly sized, dilute, aqueous aerosol therapies.