



Respiratory Disease Pharmacology Models

Validated Models

- Asthma
- COPD
- Lung fibrosis
- Lung irritancy
- Bronchodilator activity

Coming Soon

- Severe Asthma
- Cough and enhanced cough
- Tobacco smoke-induced lung inflammation
- Mucociliary clearance rates (normal and impaired)

Decisions about a respiratory discovery program must be based on robust, reproducible assays, validated with clinically relevant compounds, and used in conjunction with histopathology, inflammatory mediator analysis, and translational biomarkers.

Charles River's scientists have a solid track record of success in this area, having delivered 25 development candidates to our clients since 2000. Leveraging a wide array of well-characterized animal models of disease, qualified biomarker assays, and a variety of administration routes (including inhalation), we are uniquely equipped to profile compounds *in vivo*, or tap into our pharmacokinetic expertise to assess compound exposure within the models and drive an understanding of PK/PD relationships and aid dose-to-human predictions.

EVERY STEP OF THE WAY

Asthma Models

- Ovalbumin-induced inflammation in mouse and rat
 - **Steroid-sensitive** eosinophilia, with airway hyper responsiveness (AHR) as an optional endpoint
- Alum/house dust mite (HDM)-sensitized and HDM-induced steroid-sensitive inflammation in mouse
 - **Steroid-sensitive** eosinophilia
- *Alternaria alternate*-induced inflammation in Brown Norway rat
 - **Steroid-sensitive** eosinophilia

COPD Models

- LPS-induced neutrophilia in mouse and rat
 - **Steroid-sensitive** neutrophilia in the lung
- LPS- and fMLP-induced neutrophilia in the rat lung
- Elastase-induced lung hemorrhage in the rat

Lung Fibrosis Models

- Bleomycin-induced fibrosis in rat and mouse
 - Established time courses allow therapeutic and prophylactic dosing
 - Endpoints include histopathology, collagen deposition, lung function assessment, and assessment of inflammatory cells and mediators

Pneumonia Models

- *P. aeruginosa* acute and chronic pneumonia in rat and mouse
- *S. pneumoniae* acute pneumonia in rat and mouse
- *A. fumigatus* fungal pneumonia in rat

Multiple Routes of Compound Administration Across Multiple Species

- Systemic via multiple routes such as oral, i.p., iv.
- Inhaled via multiple routes such as aerosol, i.t., i.n., dry powder

Assessment of Bronchodilator Activity

- Lung function measurements with or without spasmogen-induced bronchoconstriction

Assessment of Lung Irritancy

- De-risks inhaled projects; aids compound, physical form, and salt selection
- Measurements of lung function, irritation (e.g., cough), local, and systemic inflammation and lung histopathology in mouse, rat, and guinea pig following dosing to the lung