



## **WORK PRACTICE AND FEATURED CASES: INTRODUCTION TO THE INHALATION LABORATORY**

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The major types of inhalation drugs include powder mist, aerosol, spray and inhalation solutions. There are huge differences in aerosol-generating devices among the various forms of inhalation drugs in the pharmaceutical development and clinical trial stages, but the administration mode to animals is basically the same in pre-clinical pharmacodynamics and toxicology assessment phases. For nonclinical studies, animal airway nebulization can be used in the early exploration stage, and the toxicology and pharmacodynamic research usually adopts oral and nasal inhalation exposure which is similar to clinical use. However, as the subjects of nonclinical studies are animals, and inhalation administration relies on the active breathing of the animal subjects, there are many uncertainties in the experiment.

**Compared with the pre-clinical assessment test of conventional drugs, the assessment of inhalation drugs requires attention in the following areas:**

- 1) Generator choice for each inhalation drug (the stability, uniformity and reproducibility of aerosol, as well as aerosol particle size and its distribution);
- 2) Adaptive training of animals and optimization of restraint conditions;
- 3) The distribution characteristics of inhalation drugs in the respiratory tissues (trachea, lung, nasal cavity), focusing on the lung-to-blood ratio and with high standards for bioanalytical methodology;
- 4) Clinical dose of inhalation drugs tend to be low with relatively less blood intake, but in preclinical assessment, in order to fully expose whole-body toxicity, the target dose is often designed to be higher, with its effective dose ratio much higher than that of other drugs;
- 5) Pay attention to the histopathological changes of nasal cavity, larynx, trachea, lungs and bronchi. However, due to the anatomical characteristics of the rodents, the histopathological changes of the nasal cavity and larynx may be less clinically relevant.

Based on the characteristics of inhalation drug research, the Inhalation Laboratory has accumulated a wealth of practical experience. At present, the Inhalation Laboratory has established a complete oral and nasal exposure inhalation administration method for large and small animals, including 12 small animal oral and nose exposure systems, 8 large animal oral and nose exposure systems, independently-developed aerosol generating device (metered dose inhaler, or MDI), powder mist generator, and liquid generator, with the capacity to conduct inhalation drug research on mice, rats, guinea pigs, dogs, monkeys and other animals. The Laboratory prides itself in its excellent technical operators, complete test product analysis and bioanalysis systems, and advanced pathology assessment team. It has the ability to evaluate innovative drugs in powder mist, aerosol and spray. As of now, the inhalation laboratory has completed full studies on the pharmacodynamics and safety assessment of 4 innovative chemical drugs, safety assessment of 1 biological drug, and safety assessments of nearly 30 generic drugs.

In addition, the Inhalation Laboratory has also established stable models of mice and rat asthma, rat pulmonary fibrosis, rat COPD, etc., with the ability to evaluate the pharmacodynamics of inhalation drug administration.