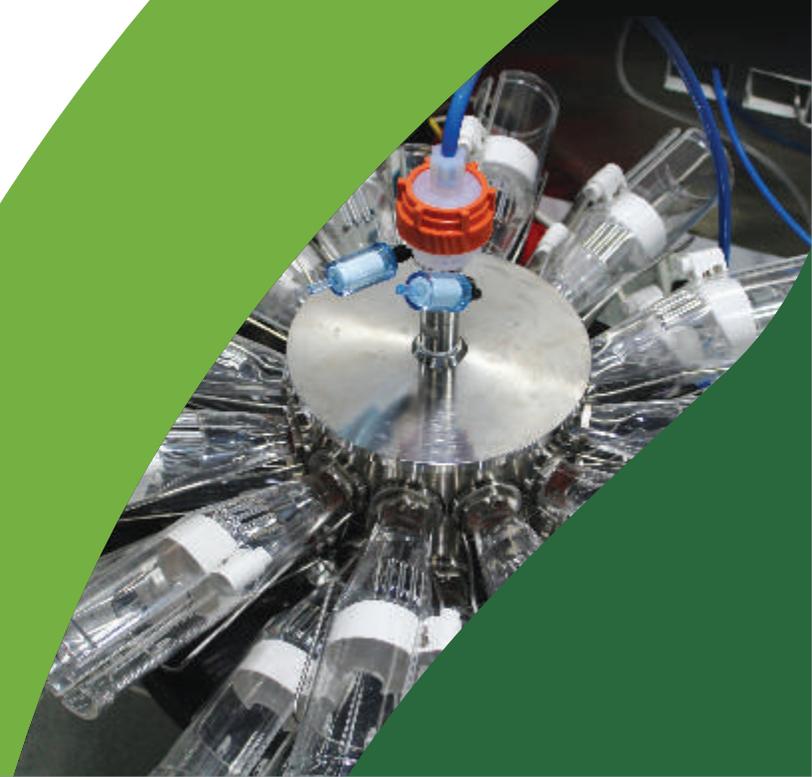




JRF GLOBAL

INHALATION TOXICOLOGY RESEARCH



Inhalation Toxicology Research at JRF



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With an increasing demand of the respiratory therapeutics, it has become an imperative subject to assess the safety of the test item or device before they are used for therapeutic indications. Typical simulated testing protocols involve exposure of rodents, as a test system, to a purpose designed sophisticated inhalation equipment. These studies are conducted in specially designed stainless steel inhalation chambers. The facility is housed in an area which receives HEPA filtered 100% fresh air. Each chamber has its dedicated facility for generation of aerosols as well as exhaust. This eliminates the possibility of cross contamination amongst doses. Each chamber houses an inhalation tower and the ancillary equipment. Each tower is connected to dedicated equipment, which control air-flow, chamber pressure, monitor temperature, humidity, and rate of air-flow through the system. Each chamber has the capacity to accommodate 10 to 64 rodent-holding tubes. The exhaust gases are stripped clean of the test item, to prevent any occurrence of accidental exposure to the researchers or the environment. All the inhalation studies are conducted in compliance with the relevant in-house SOPs and concerned regulatory guidelines.

JRF's Inhalation Toxicology Facility is designed to provide contemporary capabilities for conducting exposure of experimental rodents, under the Good Laboratory Practices (GLP). Since rodents are involved, each protocol is approved by the Institutional Animal Ethics Committee.

The facility is designed to undertake exposure of rodents to liquid, dry powdered test items, as well as different inhaler devices. On-line particle size analyser facilitates quantitative evaluation of particle size distribution. Rodents are housed in an adjacent animal room ensuring the comparable environment. This facility offers options of using diverse aerosol generation systems - spray atomiser, BLAM atomiser, collision nebuliser, etc. - to generate aerosols from different types of liquid with desired size of particles and aerosol concentration. The unique dust generation system – Rotating Brush Generator (RBG) - is dedicated to each tower, which facilitates generation of dust with minimal quantity of the test compound.

JRF has a huge experience of handling different types of chemicals. More than a thousand inhalation exposure studies have been completed in compliance with GLP and submitted to several regulators across the globe. Our studies are well-received by the global regulators.

The nose only equipment allows for higher density of rodents exposed in parallel. Figure 1 illustrates a nose only device, capable of exposing 48 rodents in one exposure tower, can be extended to 64 rodents. Chambers ensure parallel exposure under comparable environmental conditions to each group of rodents, thereby, decreasing the possibility of variability in the study results.

The exposure protocols for solids or liquids include:

- Cascade impactor for gravimetric estimation of particle size distribution
- Open face sampler for gravimetric estimation of breathing zone concentration/s
- Solvent / matrix traps, followed by extraction and quantification using analytical instruments like GC/MS, HPLC-MS/MS for accurate determination of breathing zone concentrations
- Optimisation and validation of breathing zone development at desired dose levels
- Acclimatisation of rodents to the inhalation exposure conditions
- 7/14 days dose range finder
- Main repeat dose study (4/13 weeks)



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- Development and validation of entrapment of breathing zone particles and validation of analytical / gravimetric methods
- Sample analysis, minimum three times every day for all the days of exposure
- Histopathology of respiratory organs
- Broncho-alveolar lavage (BAL) analysis
- Whole body plethysmography
- Clinical and histopathological evaluation to logically conclude the findings, such as;
 - + **Nasal cavity:** Four transverse sections - Posterior to upper incisors; incisive papilla; second palatine crest and first molar teeth
 - + **Larynx:** 3 transverse sections - Base of epiglottis; ventral pouch and cricoid cartilage
 - + **Lungs:** 5 sections - Left lobe (longitudinal horizontal); Right caudal lobe (longitudinal horizontal); right cranial lobe (transverse); right middle lobe (longitudinal vertical) and accessory lobe (transverse)
 - + **Trachea:** 2 sections - Transverse and Longitudinal at bifurcation (carina)
- Blood carboxy-haemoglobin estimation

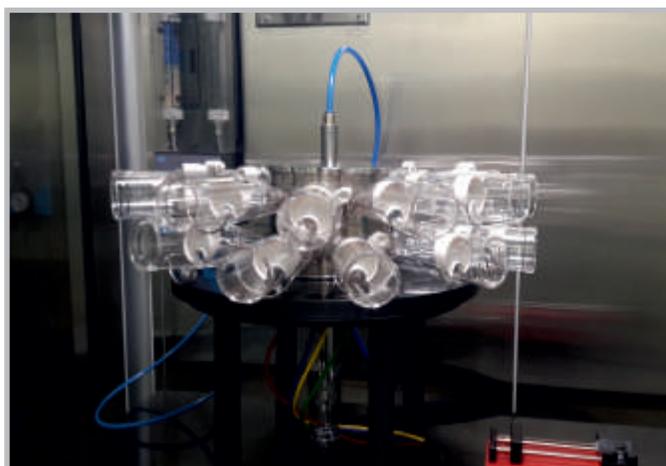


Figure 1

JRF Inhalation team consists of highly qualified, disciplined, and skilled scientists, with collective experience exceeding a few dozen years. They are ably supported by well-trained support staff, who exhibit professionalism with a personal touch.

JRF is thus, the right destination for all your needs of a high quality of science, equipment; economical, and professionally conducted single and repeated dose inhalation study for your compounds.