

# Inhalation studies

Since the importance of the inhalation route is being increasingly recognized both for chemicals and pharmaceuticals, and the materials to be tested become more and more complex, much effort is spent on developing and improving generation and analytical techniques.

The Department of Toxicology and Applied Pharmacology is actively involved in research in the area of inhalation toxicology and pharmacology both at the animal and human level. The purpose of the programme is to provide industry and regulatory authorities with adequate research methodologies for

identifying and evaluating effects resulting from inhalation exposure to chemicals or pharmaceuticals. As a result, the Department offers custom-made designs for hazard evaluation and risk assessment with quick and reliable generation and monitoring systems for gases, vapours and aerosols.



**TNO offers custom-made study designs for hazard evaluation with quick and reliable generation and monitoring systems for gases, vapours and aerosols.**

## Facilities

An area of about 600 square meters houses more than 25 nose-only exposure units and whole body inhalation chambers, animal rooms, a workshop, an area for safe dismantling and cleaning of inhalation exposure units, and rooms for undisturbed behavioural assessments of exposed animals.

## Generation and control of test atmospheres

- (Semi)automatic generation monitoring of gases and vapours
- Aerosol characterization
- Fully equipped chemical analysis laboratory

## Other methods to expose the respiratory tract

- Intranasal application
- Intratracheal instillation

## Guideline tests

- Acute, subacute and subchronic inhalation
- Chronic inhalation / carcinogenicity
- Sensory irritation (Alarie test)
- Augmented acute (including lung function and histopathology)
- CxT (determination of concentration-time response relationships (probit relations) following acute exposure)
- General and/or Safety Pharmacology (to investigate effects on airways)

These studies can be performed in different species (rats, mice, hamsters, guinea pigs, mini pigs, rabbits, dogs) and are conducted in compliance with OECD, EC, US EPA (FIFRA/TSCA), US FDA, EMEA/ICH, Japanese MITI, MAFF and MHW guidelines.

### Special resources

- Facilities for human experimental inhalation exposure
- Combination with reproduction, immunology or neurobehavioural/neuropathology studies
- Combination with genotoxicity and cytotoxicity studies *in vitro* and *in vivo*
- Pharmacokinetic/toxicokinetic studies
- Tiered approach for respiratory allergenicity testing

### Quality

- GLP certification
- Over 40 years experience in contract inhalation studies
- Research staff with extensive experience in contract inhalation studies and in basic research
- Ample experience in consultancy and evaluation

### Research programme

- Health effects of exposure to nano-particles
- Development of acute and chronic asthma models
- Ongoing development of lung function measurements in rodents
- Development of measurement of minute ventilation in dogs during exposure



*In vitro model using a gas mixing chamber to expose nasal turbinates, tracheal tissue and nasal cells to gases under continuous monitoring.*

### Advanced methods/techniques

- Closed chamber uptake studies including PbPk modeling
- Exposure of cell and/or organ cultures of nose, trachea and lungs
- Exposure of lung slices of different species including man
- Bronchoalveolar lavage (BAL) plus determination of specific components
- Genomics/transcriptomics

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