Inhalation

Exposure Systems

Advanced Toxicology Studies

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About Us

We design, develop and manufacture in-vivo and in-vitro inhalation systems, used for long- and short-term investigations into pharmacology, toxicology, environmental and occupational safety, in compliance with **OECD, EPA and GLP guidelines**. Benefitting from over **40 years of being in the inhalation research field**, we work together with the customer to design equipment specific to their application and scientific research needs.

Design Consultation: The most successful projects begin with collaboration. TSE Systems' Inhalation experts work with the customer and multidisciplinary teams to understand design configurations and/ or constraints. Together, they work on safety assessment protocols and methodologies for measuring the physical-chemical properties of the test substance. Training and scientific support are provided during the system installation and set-up.

Exposure chambers: Head Nose Only, Whole Body and Cell Culture units are available in a wide range of sizes and designs, for mice to large animals as standard.

Application: Liquid and dust aerosols; vapors; cigarette smoke as well as numerous customer specified applications. According to the system requirements, the modular design permits working alternatively with different substances.

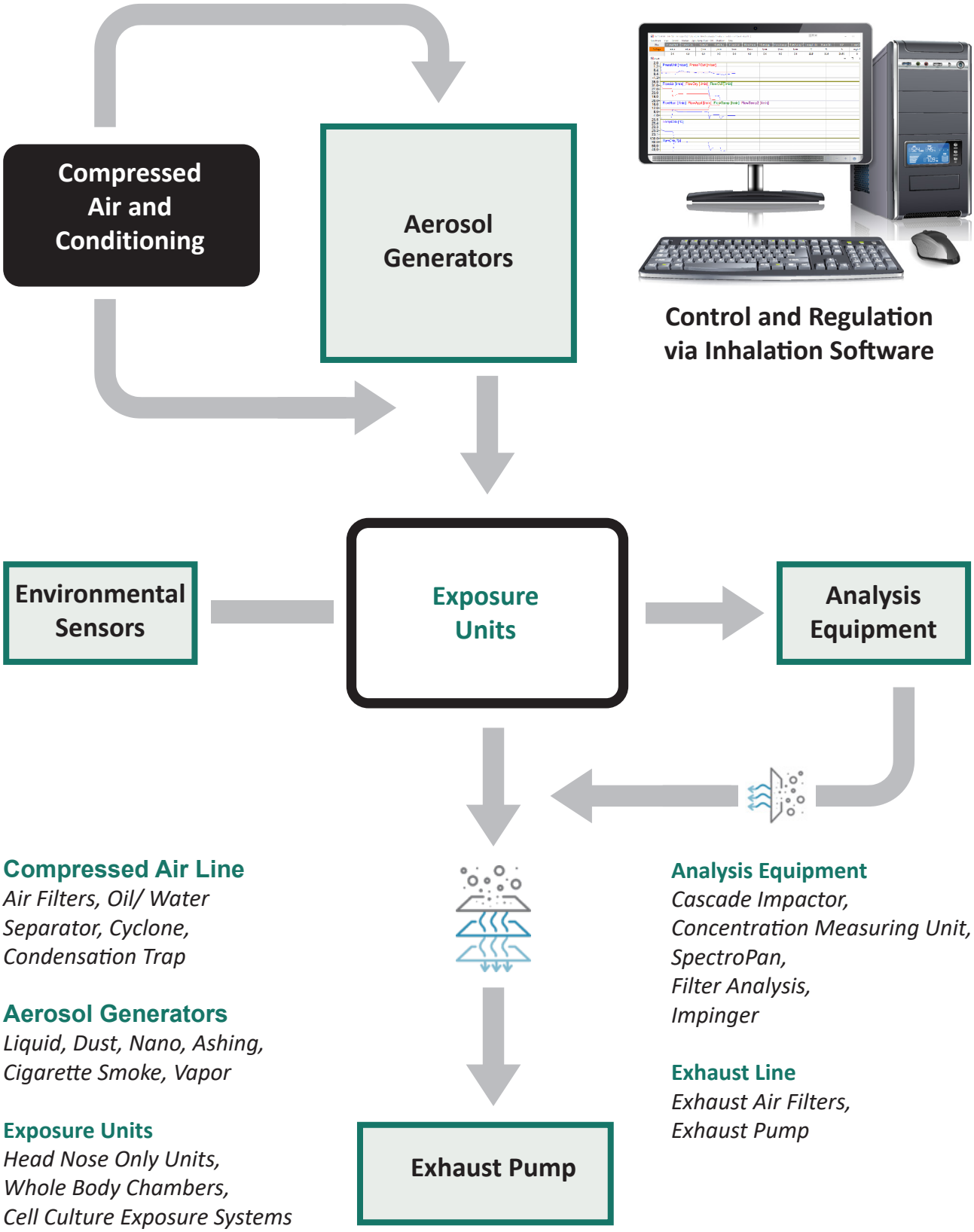
Experiment control and analysis: The complete system is controlled, regulated and monitored, fully automatically with TSE Systems inhouse Inhalation Software (DACO), which additionally logs all data parameters. We offer real-time and/ or offline analysis equipment suitable for your substance of interest, quantifying concentrations continuously.

Support: In the initial stages TSE Systems provides expert consultation for optimal system installation in the laboratory. Aerosol and vapor generation is adapted to the physical-chemical properties of the test substance, with individual solutions for substances difficult to aerosolise.

MADE IN GERMANY

Part 11 Compliance

Inhalation System Overview



Compressed Air Line
Air Filters, Oil/ Water Separator, Cyclone, Condensation Trap

Aerosol Generators
Liquid, Dust, Nano, Ashing, Cigarette Smoke, Vapor

Exposure Units
Head Nose Only Units, Whole Body Chambers, Cell Culture Exposure Systems

Analysis Equipment
Cascade Impactor, Concentration Measuring Unit, SpectroPan, Filter Analysis, Impinger

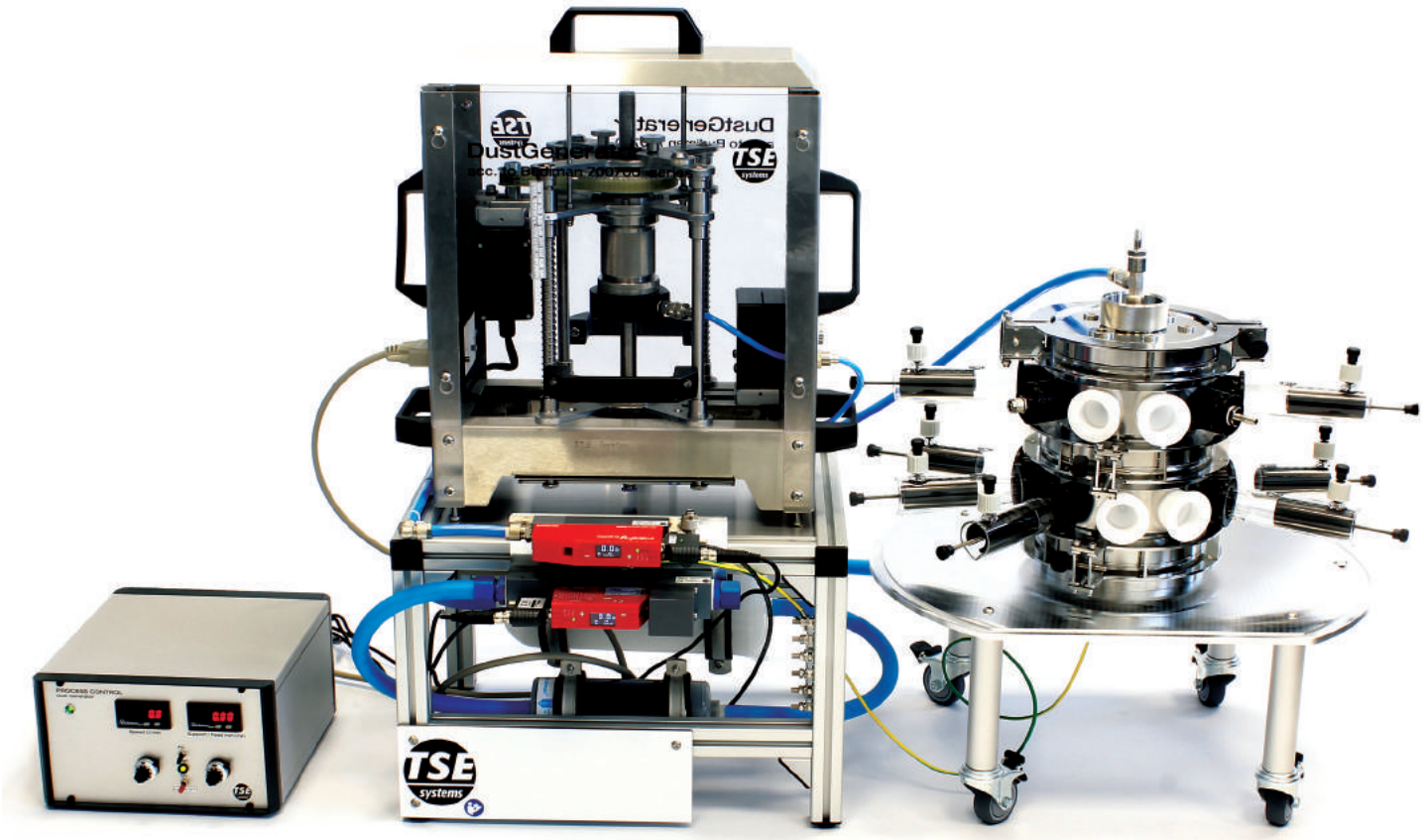
Exhaust Line
Exhaust Air Filters, Exhaust Pump

Table Top Systems

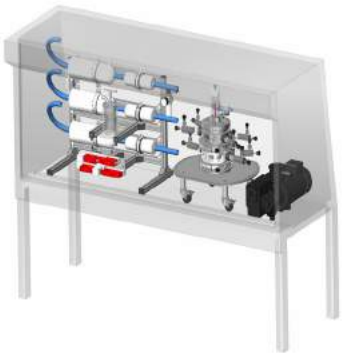
The new Table Top Inhalation System from TSE Systems is a fully integrated, high-precision measurement system for fast, reproducible measurements with a reduced setup time.

TSE Systems *NOW* offers a head nose only exposure unit that fits size requests and **budget constraints**. A must have for researchers interested in pioneering preclinical discoveries. This compact and modular design offers a fully integrated, high-precision exposure unit for **8 to 26 rodents**, with a lower internal volume to minimize substance use rounded off with a reduced set-up time.

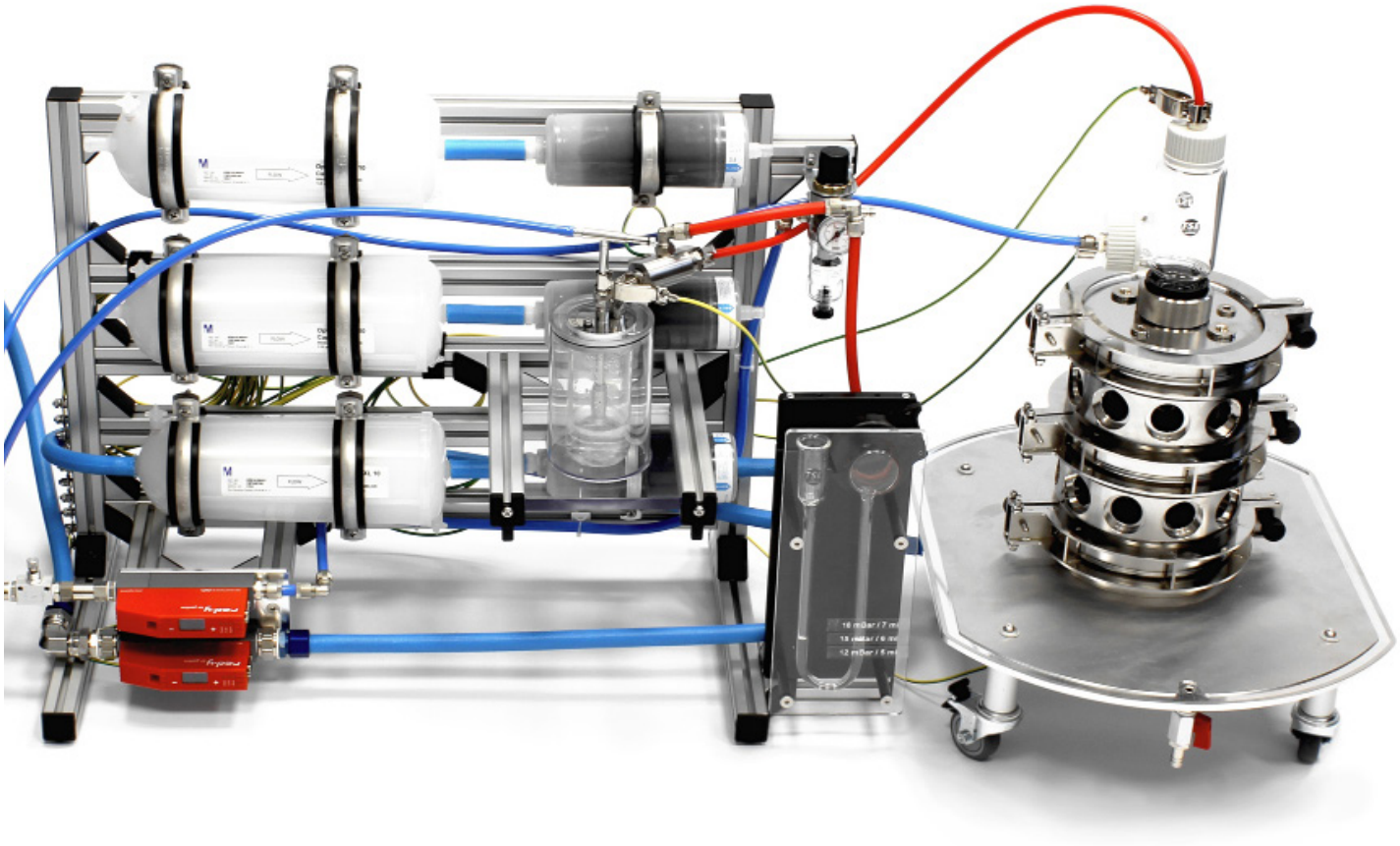
With its compact size and low budget, this innovative solution enables preclinical researchers and start-up laboratories to pursue their toxicology studies, with an array of substance generation possibilities e.g. **liquid, dust, vapors, cigarette smoke**.



Designed to operate in a standard fume hood, the table top system is rounded off by having the flexibility to choose between a **semi- or fully-automatic system**. The fully-automatic version has a state-of-the-art inhalation software, designed for the collection of both measurement and logged data from the environmental sensors and mass flow controllers which monitor and control the system.

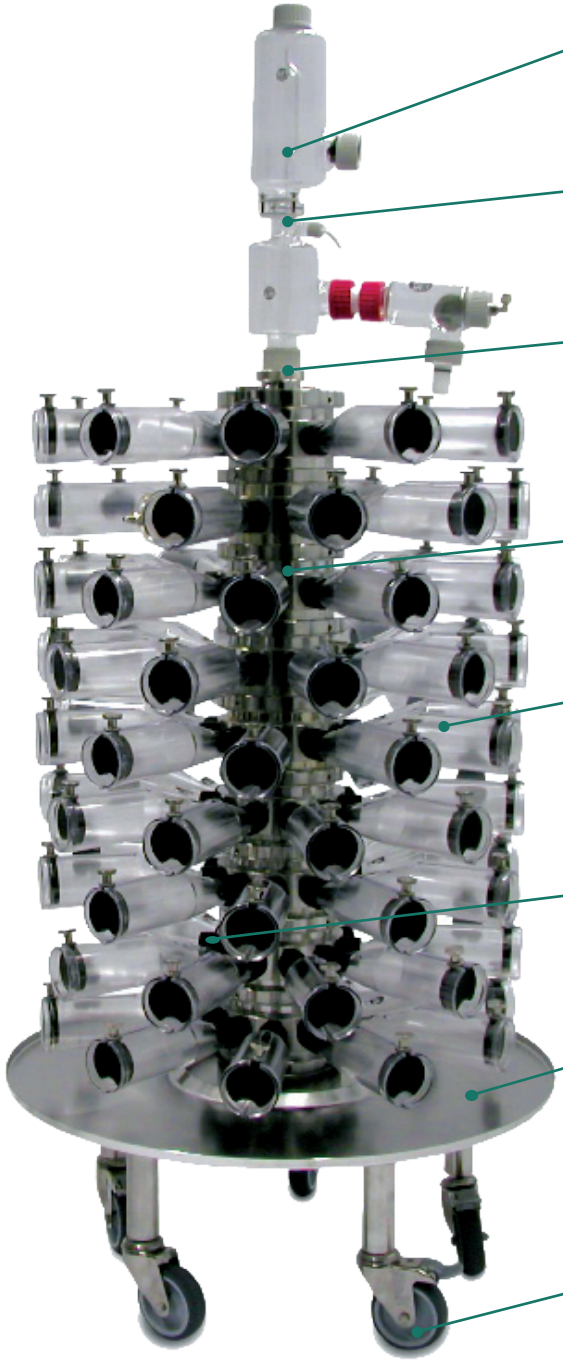


This new Table Top Inhalation System is a must for pioneering preclinical toxicological studies, not only for now but as a **foundation for the future**!



Head Nose Only Units

The modular expandable design uses single segments stacked upon one another, enabling 8 to 96 animals to be exposed simultaneously. Each Head Nose Only exposure unit can be equipped with the required aerosol inlet interfaces, appropriate exposure tubes, various sampling ports and environmental sensor connections. The restrainer construction is designed for simple operation, quick replacement and easy cleaning, for a wide range of species – mouse up to guinea pig size as standard.



Preparation of large aerosol particles via preseparator and/ or cyclone

Low sample consumption and re-collection – particularly advisable for highly toxic or expensive test substances or when the test substance is in short supply

Test atmosphere flows into an inner plenum that directs the flow towards the nose or head of each test animal via a directed-flow design

Exhaled air is then discarded along with the excess airflow into an outer plenum

Restrainer construction is designed for simple operation, quick replacement and easy cleaning, for a wide range of species

Restrainer/ Sampling ports for e.g. a concentration measuring unit, impactor and/ or sample filter analysis

Excrement tray for easy collection and disposal of animal feces – easy to clean

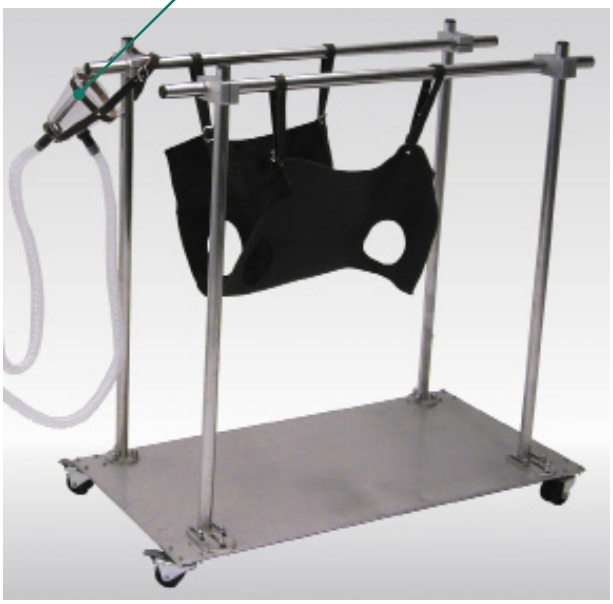
Mobile versions or standing versions for walk in fume cupboards, or compact versions for table top designs are available

Snout Only Units

Special solutions for animals larger than rodents e.g. dogs and non-human primates. Test substance administration is possible by using face masks of different sizes. The standard units are designed for flow rates of up to 6000 l/h – higher flows are possible if required – and mobile animal holding equipped with comfortable leather harnesses.

Features:

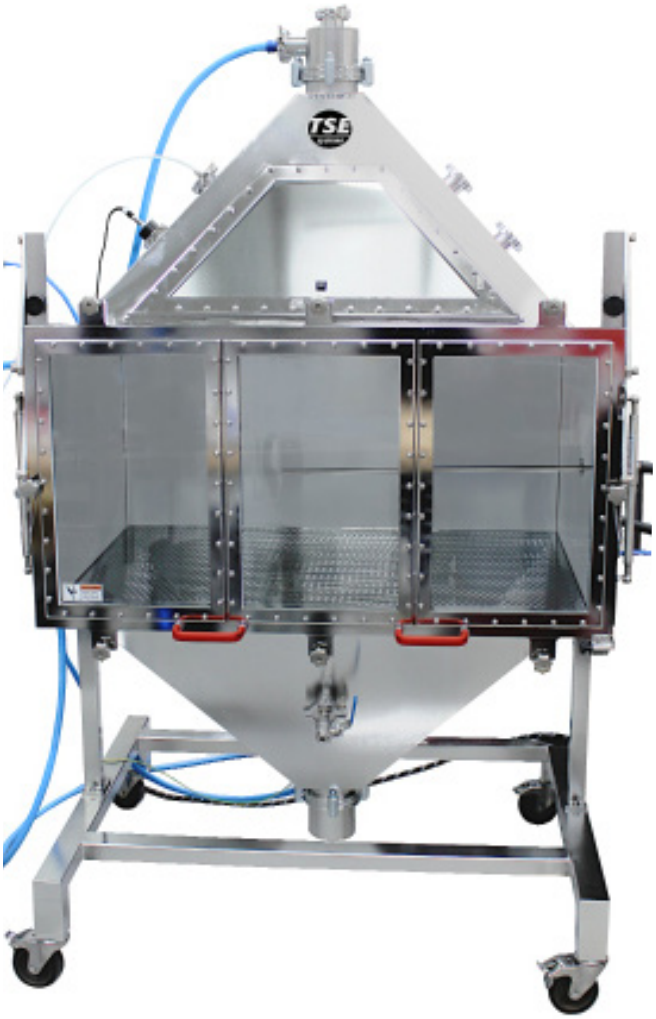
- Different mask sizes for small to large dogs with the proven directed-flow design
- Spatial separation of fresh and exhaled air – minimal rebreathing of exhaled air
- Central aerosol administration via various preconditioning units available as standard
- Sample ports and sensor connections available in both the upper and lower cylinder

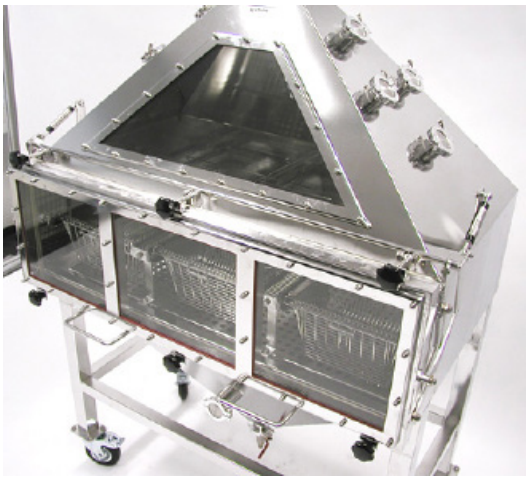


Whole Body Chambers

Simulating real exposure conditions for a wide range and large numbers of animals, either under dynamic and/or static conditions. These whole body exposure units are available in three sizes as standard (0.05, 0.6 and 1 m^3) as well as custom-made sizes.

Homogeneous test substance and optimal flow distribution is guaranteed by a **proven aerodynamic design** – i.e. square cross-section with pyramidal end caps. The technical execution of the chambers is adapted to suit the large throughput volume of the test atmosphere.





Options:

- Variety of standard sizes of stainless-steel cages
- Several types of cage carrier racks are available for the highest degree of flexibility
- Customized specifications such as numbers of sample ports and special seal materials according to the type of test atmosphere can be implemented
- Provision of drinking water and additional sample ports can be realized where required

Features:

- Large viewing port(s) made from safety glass for animal observation
- Safety valves for exceeded under or over pressure
- Airtight according to the international standard ISO 10648-2
- Mounted on a mobile rack for easy positioning

Cell Culture Exposure Systems

An efficient, user-friendly tool for supplementing and amplifying inhalation research programs in inhalation toxicology and screening tests. It is perfectly suited for comparing *in vitro* and *in vivo* data by using modular components from our inhalation systems including generators, humidity control systems and various analytical instruments.

Features:

- Each exposure unit is suitable for 2 standard culture plates with 6, 12 or 24 wells, with Air Liquid Interface (ALI) membrane inserts
- Compatible with cell culture plates von various manufactures including Transwell®, Costar®, Corning®, TPP®, Greiner® and Falcon®
- Exposure of the wells, via an internal flow plate for equal and consistent dispersion
- Integrated heating, atmospheres with high CO_2 content and humidification can all be implemented

Environmental Sensors

Pressure sensors for the exposure unit and filter monitoring; also, as chemical-resistant versions

Temperature and Humidity sensor; humidity data can be linked to a humidification generator for optimal and automatic re-humidification of the exposure unit's air

Oxygen and Carbon Dioxide sensors with high gas specificity and long-term stability

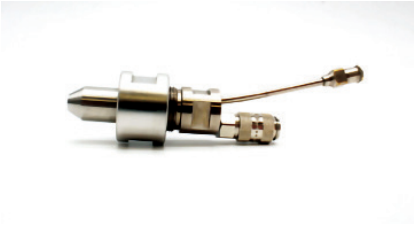
Special sensors, e.g. for carbon monoxide, ozone, Volatile Organic Compounds (VOCs) such as benzene, etc., are additionally available for real-time exposure monitoring

Calibration kits, including calibration gases, a pressure calibration unit, humidity testing sets, flow meters etc. are provided according to the systems requirements

Our in-house **Daco Inhalation Software** enables the calibration of sensors for the highest measuring reproducibility

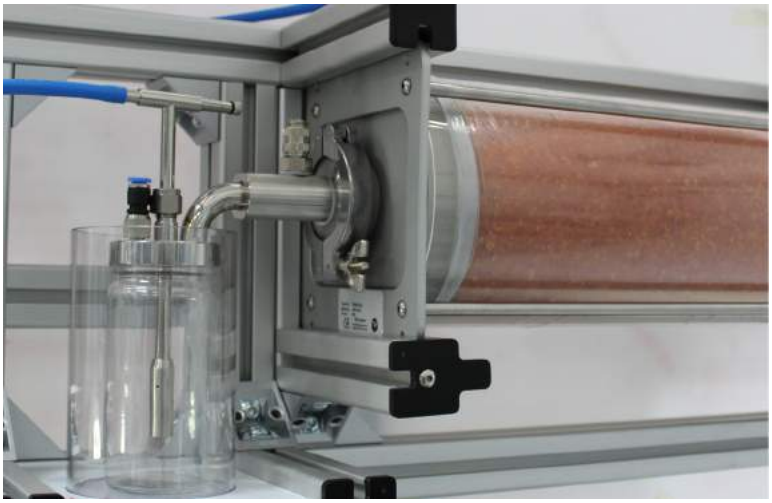
Liquid Generators

Several generators are available for the nebulization or vaporization of liquids such as aqueous solutions. All the generators can be equipped with adapters for connection to either the Aerosol Conditioning or Exposure Units or used with third-party items. For each generator, appropriate dilution or conditioning units are available to adapt the aerosol or vapor properties to the test requirements.



Essential features of the **Aerosol Nozzles** include, substance mixing immediately before dispersion, constant aerosol composition (no concentration changes in the reservoir). The nozzles special design enables an air-liquid mixing procedure optimal for the creation of droplets with a diameter less than 3 µm. It is also suitable for challenging liquids with a high-viscosity these can be dispersed into the test atmosphere by using a heated aerosol nozzle.

Ultrasonic Nebulizers convert electrical energy into mechanical vibrations. Due to these particularly fast vibrations, the smallest particles of the inhalation liquid become detached. Especially for the application of small amounts of aerosol and for research into inhaled medications Ultrasonic Nebulizers are suitable. Equipped with a disposable substance container so that there is minimized test substance contamination by residues from previous tests.



The combination of a **Collison Nebulizer** - suitable for loss-free nebulization from a liquid reservoir (which can be refilled while the test is running), together with an **Aerosol Drying Unit** - which reduces droplet size through evaporation, can efficiently be used for Nano Particle Generation (**NanoParticleGenerator**).

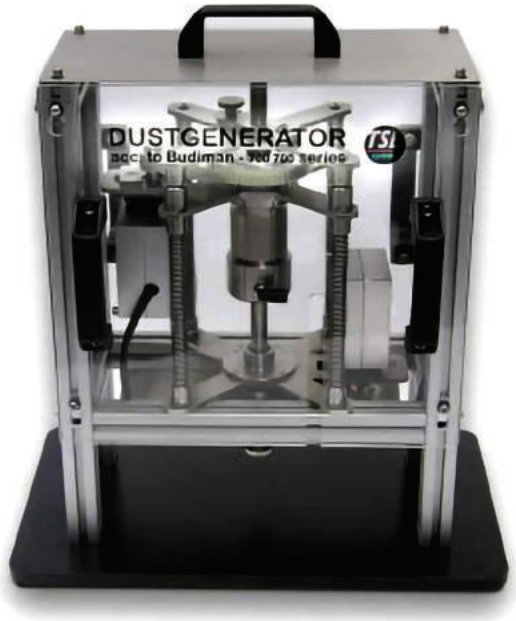
The individual and computer-controlled operation of 16 Metered Dosed Inhalers (MDIs) simultaneously is possible using our **MDI Activator-16**. The additional software module integrates into our inhouse inhalation software (DACO), controlling and monitoring all the parameters necessary, such as shaking time, activation time, pause time, filling activators and activation pattern for optimal application planning.

Aerosol Conditioning Units offer the best solution for refining particle properties and adjusting the substance concentration according to the experimental design. The conditioning units are made of high-quality laboratory glassware or other resistant materials such as stainless steel or special plastics. High flexibility through adaptation of conditioning units to individual test designs on request and solutions for connection to different Exposure Units are possible.

Dust Generators

Two designs are available with specific principles for either dry substances suitable for compaction into a cake or for loose materials convenient for long-term tests, thus allowing a range of applications:

- Short or long exposures
- High or low dust concentrations
- Manual or automatic mode by using a feedback loop to the systems concentration measuring unit and our inhouse inhalation software (DACO).



Dust Generator acc. to Budiman

are designed for working with finely powdered and dry substances, that can be compressed to dry dust cakes via a Hydraulic Press provided optionally. This generator is a further development of the well-known Wright dust feeder, made from robust, wear-resistant material, operating with an exact and accurate mechanism. The dust reservoir advances on a stability platform towards the scraper, while the scraper is rotated on a central axis. The dust is removed from the scraper through the axis and is dispersed and mixed before being passed, into the exposure unit.

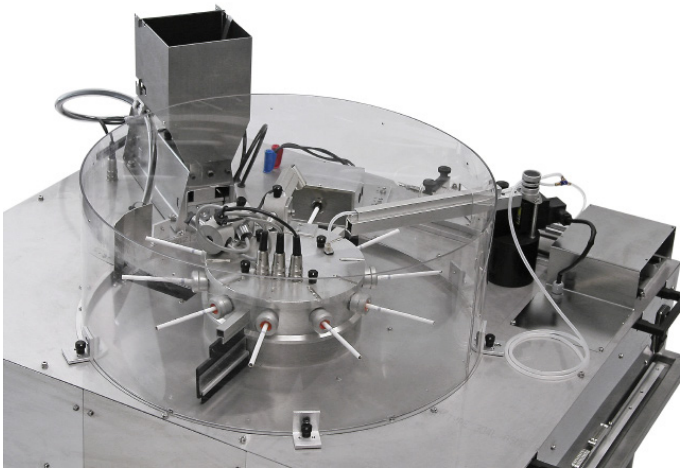
Dust Generator acc. to Bundschuh

are designed for use with loose materials and for generating high aerosol concentrations as well as for long-term tests. It has been designed to disperse amounts from 10 g to 550 g per hour and can also be used with finely ground fibrous substances, without previous test substance compression. The substance reservoir is equipped with a stirrer and ventilation for continuous dust conditioning during the experiment and the test substance is dispersed by a venturi nozzle which is driven by compressed air.

Other Generators

Through multi-disciplinary collaborations with experts from leading research institutes and universities, TSE Systems developed **Nanoparticle Generators** and analytical instrumentation for research into inhalable nanoparticles. Moreover, user-specified generators for the generation of test atmospheres such as **Ozone Generators**, **Ashing Generators** as well as those for volatile organic compounds - **VOC Generators** such as benzene, hydrocarbons, etc. A standard exotic generator remains the **Cigarette Smoke Generator** designed for generating cigarette smoke for analytical and experimental investigations such as COPD studies into health damage caused by cigarette smoke. Both cigarette smoke generators offer a smoking routine and puff profile according to DIN ISO 3308 and other protocols.

VOC Generator



Cigarette Smoke Generator 10-port

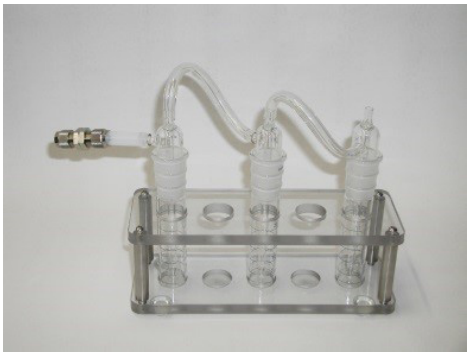
Ozone Generator

Offline and Real-time Analysis

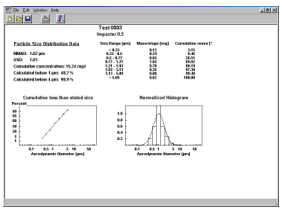
A complete range of instruments for offline and real-time analysis according to the design of the exposure system and the particle properties of interest. The spectrum ranges from basic equipment to the most sophisticated available optical instruments for the determination of particle properties. Automated sampling routine and data storage is one of the many features offered. Our inhouse inhalation software (DACO) and special analysis software can be used as a tool for the calculation of particle size distribution with data from cascade impactor sampling.

Filter Analysis - a gravimetric determination of particle concentration via weight of substance collected. According to the particular test substance used, different filter materials such as glass fiber, quartz fiber, PTFE, or cellulose nitrate in reusable filter capsules can be used. Concentration analysis is also possible by subsequent analytical methods such as HPLC, fluorescence spectroscopy, etc.

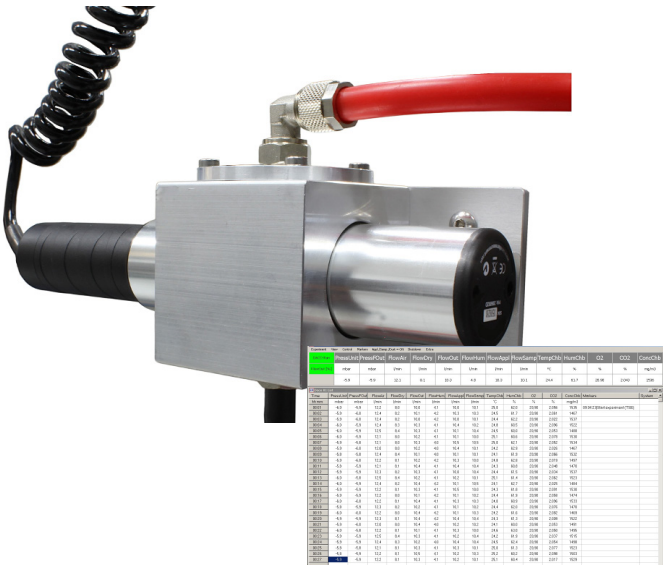
Midget Impingers - bubblers/ bottles connected to an air sample pump to collect airborne samples which are designated into collection liquids for analysis. A rack is also supplied perfectly matched to the size of the midget impingers for support and stability, suitable for up to five midget impingers in total.



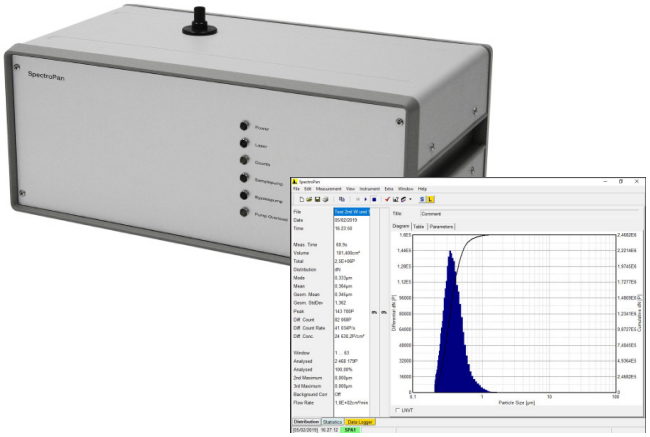
Cascade Impactors - Mercer style 0.5 and 6 l/min cascade impactors are available for determining the particle size distribution and the mean mass aerodynamic diameter MMAD as well as the aerosol concentration. A particle size distribution software program is also available for the computer-supported evaluation of impactor analyses data.



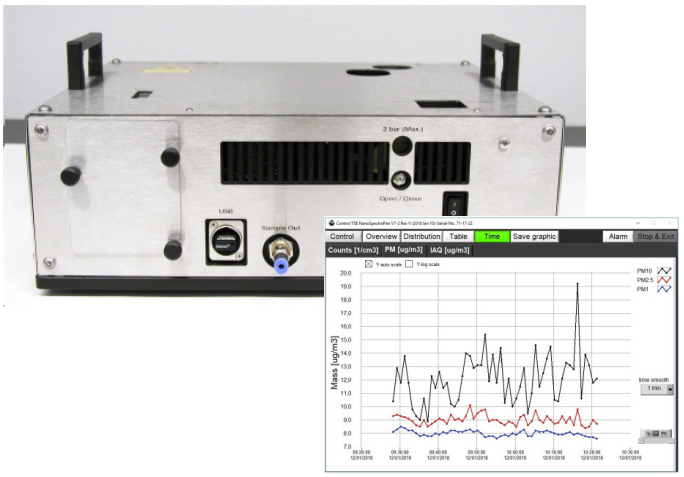
Concentration Measuring Unit - a robust, compact, data-collecting measuring device for the real-time recording of airborne dusts, fumes and aerosols. The CMU uses a light scattering principle to make accurate and repeatable measurements. The CMU is factory calibrated using ISO 12103-1 Fine Dust Test and each unit is supplied with its own unique calibration insert which creates a known optical scattering effect in the sample probe's chamber.



Particle Size Distribution (SpectroPan) - a real-time analysis system for various applications recording particle size and number distribution, particle diameter and aerosol concentration. A comprehensive software package for determination of particle size properties (e.g. distribution, number, surface, PM2.5, PM5, PM10) and concentration, including statistics functions is also provided.



Nanoparticle Size Distribution (NanoSpectroPan) - for simultaneous and precise real-time monitoring of both micron-sized and nano particles. This state-of-the-art system combines optical and electrical particle detection in one single device, enabling the monitoring of dust aerosols and nanoparticles. The combination of these two measurement procedures results in a particle size distribution in the ultra-wide particle size range from 10 nm to 35 µm, simultaneous PM1, PM2.5, and PM10 measurement with 41 high resolution particle size channels.



DACO Inhalation Software

A customizable, user-friendly and comprehensive program for inhalation studies with exposure systems. Our software is available as single or multi-place versions, the latter allowing control and data recording for several similar exposure systems via a single computer.

The software is adapted to the system configuration – covering both simple systems with basic equipment as well as complex system assemblies with extensive peripheral devices.

Various safety features such as automatic and manual shutdown for both rapid and safe system shutdown, as well as the setting of alarm limits for crucial system parameters, such as flow and pressure, are part of the standard version of the software. Software extensions for extended systems are available on request.

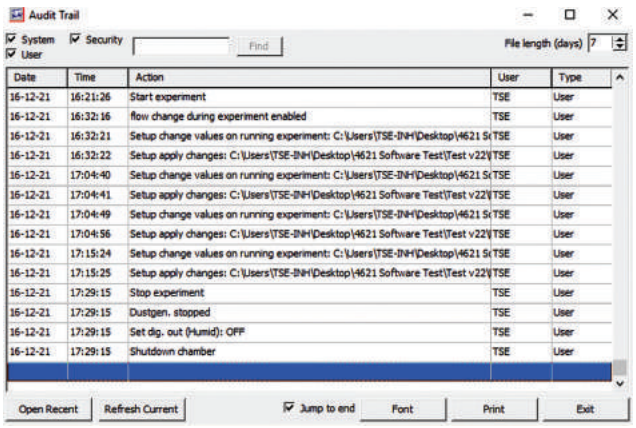
Features

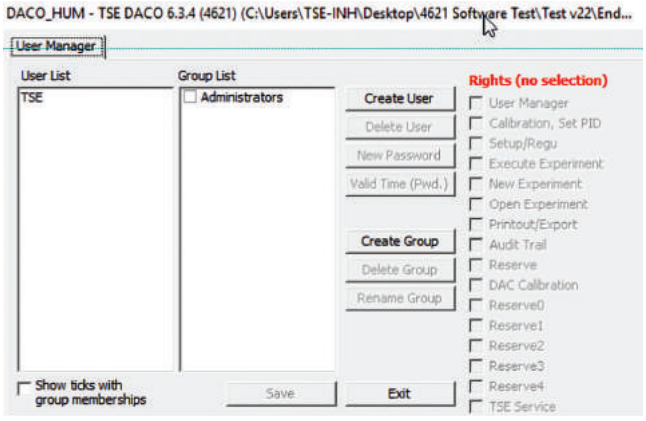
- Easy and quick planning of experiments and setting of experiment parameters
- Clearly arranged representation of data in tables or graphic displays
- Display of system status and measurement data while test is taking place
- Setting of alarm limits for system parameters
- Safety features such as automatic shutdown and emergency stop
- Separate setting of regulation functions for pressure, temperature and humidity

GLP DACO Inhalation Software

Good Laboratory Practice (GLP) is a quality regulation, which looks at the organisational process and the conditions under which non-clinical studies are planned, performed, monitored, recorded, archived and reported. The GLP DACO Software supports these guidelines with additional software modules:

- Audit trail for the automatic recording of GLP-relevant test data. All entries are logged by the system with the corresponding time and date.
- User Manager for restricted access and allocation of rights, in addition password-protected where necessary.
- Saving of calibration data in a special file. Additional saving of calibration data together with the associated sensor raw data for a measurement.
- Protection against subsequent manipulation of raw data through a special data file format.





TSE Validation and Documentation Support can also be implemented on request, including the creation, supply and protocolling of the **Installation (IQ)** and **Operation Qualification (OQ)** documents. In addition the Software Validation documentation for any TSE Software purchased can been included.

Safety cabinets and hoods

Depending on the standards required, we offer various designs of air tight safety cabinets and enclosures to secondary cubicles and hoods for spatial separation. Fume cupboards especially designed for a particular system can also be manufactured on request.

The interior designs provide supports for exposure instrumentation, fixing units for measurement devices and the holders for the exhaust filters of the inhalation exposure system. Compact design and mobility through mounted wheels increase flexibility and helps equipment transportation.

Enclosure – for Head Nose Only Systems

Mounting Panel (back) – compact, collection of essential components

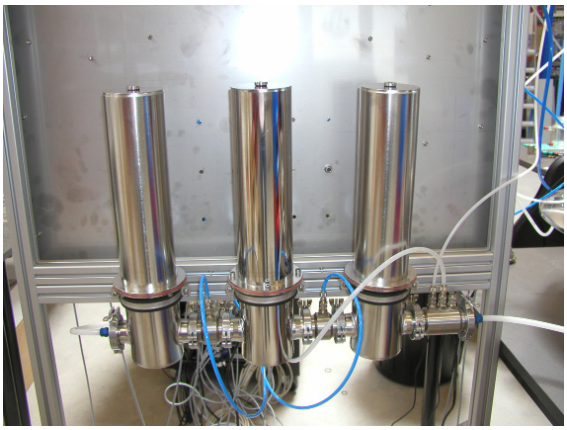
Hood, Mounting Panel (front) – Generators with additional filter system

Essentials

Turnkey systems are only possible through expert knowledge, modular systems and high-integration, providing everything you need from the beginning to the end of your research needs. We do not only manufacture the critical components of an inhalation system but everything in between. From compressed air and its conditioning for a higher classification of air, mass flow controllers for controlling the air flow through the system, re-humidification as well as test air conditioning, right the way through to filtration and removal of air from the system via vacuum pumps, we provide it all, everything you need!

Air Conditioning Panel – compressed air filtration

Humidity Generator – air re-humidification



Filter System – 3 stage exhaust air filtration

Selected Publications

• W. Zhang, X. Song, L. Zhai, et. al., Complete Protection Against Yersinia pestis in BALB/c Mouse Model Elicited by Immunization With Inhalable Formulations of rF1-V10 Fusion Protein via Aerosolized Intratracheal Inoculation. Front. Immunol., 13, 793382 (2022).

• S.-C. Hu, S. Min, H.-K. Kang, et. al., 90-day nose-only inhalation toxicity study of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in Sprague-Dawley rats, Food and Chemical Toxicology, 160, 112780 (2022).

• S.N. Andriamasinoro, D. Dieme , C. Marie-Desvergne , et. al., Kinetic time courses of inhaled silver nanoparticles in rats, Arch Toxicol, 96 (2022) 487–498.

• L. Saveleva, P. Vartiainen, V. Górová, et. al., Subacute inhalation of ultrafine particulate matter triggers inflammation without altering amyloid beta load in 5xFAD mice, Neurotoxicology, 89 (2022) 55–66.

• A. Noël, Z. Perveen, R. Xiao, et. al., Mmp12 Is Upregulated by in utero Second-Hand Smoke Exposures and Is a Key Factor Contributing to Aggravated Lung Responses in Adult Emphysema, Asthma, and Lung Cancer Mouse Models. Front. Physiol., 12, 704401 (2021).

• R. Świercz, M. Stepnik, The effects of 1-Methylnaphthalene after inhalation exposure on the serum corticosterone levels in rats, International J. of Occupational Medicine and Environmental Health, 33, 5 (2020).

• T. Vo, K. Paudel, I. Choudhary, et. al., Ozone exposure upregulates the expression of host susceptibility protein TMPRSS2 to SARS-CoV-2, Sci Rep 12, 1357 (2022).

• D. Stanford, H. Kim, S. Bodduluri, et. al., Airway remodeling in ferrets with cigarette smoke-induced COPD using µCT imaging, Am J. Physiol Lung Cell Mol Physiol, 319 (2020) L11–L20.

• J. Yi, M.G. Duling, L.N. Bowers, et. al., Particle and organic vapor emissions from children's 3-D pen and 3-D printer toys, Inhal Toxicol, 31, 13-14 (2019) 432–445.

• J. Milara, L. Díaz-Platas, S. Contreras, et. al., MUC1 deficiency mediates corticosteroid resistance in chronic obstructive pulmonary disease, Respiratory Research, 19, 226 (2018).

• N.V. Zaitseva, M.A. Zemlyanova, Research on acute toxicity of nanodisperse manganese oxide aerosol for predicting health hazards for workers and population under inhalation exposure, Health Risk Analysis, 1 (2018) 89–97.

• B.W. Lewis, R. Sultana, R. Sharma, et. al., Early Postnatal Secondhand Smoke Exposure Disrupts Bacterial Clearance and Abolishes Immune Responses in Muco-Obstructive Lung Disease, J. Immunol, 199 (2017) 1170-1183.

• J.E. Phillips, X. Zhang, J.A. Johnston, Dry Powder and Nebulized Aerosol Inhalation of Pharmaceuticals Delivered to Mice Using a Nose-only Exposure System, J. Vis. Exp., 122, e55454 (2017).

Our system comes with all-in-one warranty and excellent technical support service

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