Advanced in vitro exposure systems

Engineering meets Cell Biology
Evaluate human health effects

VITROCELL® SYSTEMS

This is VITROCELL®

Groundbreaking technology from the heart of the Black Forest in Germany

- The VITROCELL team of 30 qualified professionals ensures delivery of unparalleled solutions to customers worldwide.
- Our technical support provides dedicated service to our customers worldwide. This commitment has made us the preferred choice of numerous renowned environmental research institutions, chemical industries, pharmaceutical companies, tobacco and e-cigarette manufacturers, and regulatory authorities.
- Nearly 300 publications covering a wide range of applications.
- The numerous and unprevailed number of VITROCELL installations around the world are proof of our expertise and the trust of our customers.
- Our users take advantage of the most comprehensive product portfolio for all applications.
- Design, production and service are in one hand to provide excellent solutions to the research community.

VITROCELL® SYSTEMS

VITROCELL Exposure Systems for Inhalation Toxicology

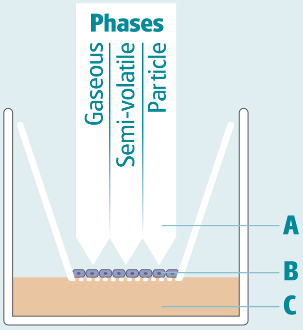
Direct Exposure Technology at Air/Liquid Interface

Air / Liquid Exposure

A Direct and controlled exposure of test atmosphere to cells

B Cells on membrane

C Media below cells



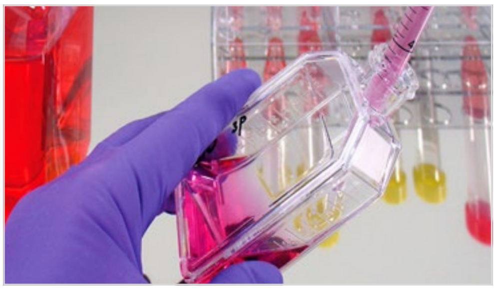
In response to the scientific need to expose in physiologically relevant conditions, VITROCELL exposure modules have been specifically designed and engineered to enable direct exposure of mammalian cells or tissue at the Air/Liquid Interface where the cell systems are not covered with culture medium.

Researchers can thus use all cell types cultivated on microporous membranes.

This approach allows for more credible and authentic results than by submerged exposure due to a closer replication of the human physiology.

The advantages

- **No losses**
- **No dissolution**
- **No reaction of constituents with culture medium**
- **High sensitivity**



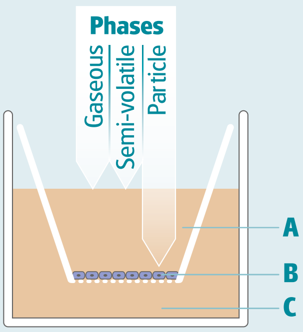
Disadvantages of submerged exposure

Submerged cultivation and exposure in incubator

A Medium above cells

B Cells on membrane

C Media below cells



The exposure of mammalian cells or tissues to airborne substances is frequently performed under submerged conditions. In doing so, the test substances are dosed into the culture medium. This procedure results in an undesired interaction of the formerly airborne substances with the medium, causing limitations for authentic analysis.

Therefore VITROCELL recommends the Air/Liquid Interface exposure technology.

Application Areas for in vitro Inhalation Toxicology

Environmental Health

- Air quality monitoring: Assessment of indoor and outdoor pollutants with long-term sampling >24 h
- Occupational health: Workplace exposure
- Public health: Pollution in urban areas

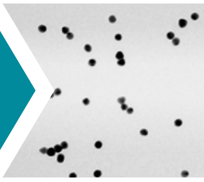
Pharmaceutical Evaluation

- Drug development for respiratory diseases: Assessment of inhalable therapeutics
- Drug delivery via liquid or dry powder aerosols
- Nanomedicine and advanced therapies

Tobacco and E-Cigarette Testing

- Safety assessment: Toxicity profiling
- Product development and comparison
- Regulatory compliance
- Harm reduction assessment

Nanomaterial Safety



- Safety and risk assessment: Toxicity profiling
- Occupational safety: Workplace exposure
- Consumer product safety: Regulatory compliance, product testing

Bacteria and Virus Research

- Bacterial and viral pathogenesis
- Antiviral drug testing on airway tissues
- Inhalable vaccine development and evaluation
- Transmission studies: Aerosol stability

Chemicals and Pesticides

- Hazard identification: Dose–response assessment
- Regulatory compliance
- Environmental and occupational safety

Cosmetics

- Ingredient safety assessment: Toxicity profiling, respiratory sensitizers or allergenicity testing
- Occupational and manufacturing safety
- Regulatory compliance under 3R strategy

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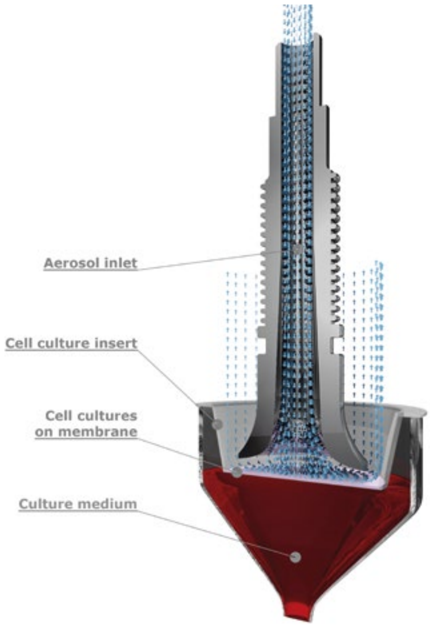
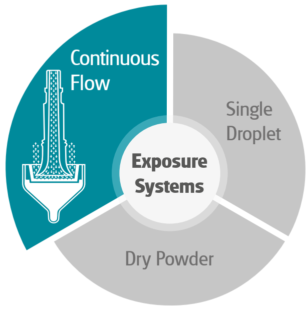
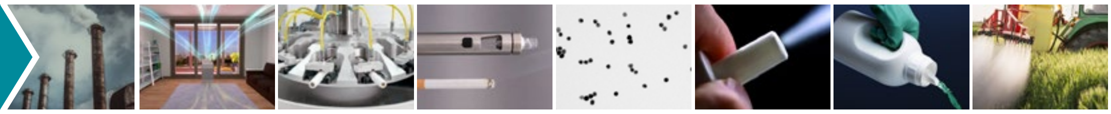
Exposure Principle 1: Continuous Flow Exposure

When using the Continuous Flow Exposure systems, cell cultures are exposed to a continuous flow of gases, complex mixtures or particles. Only this exposure principle is suitable for aerosols containing a gas and particle phase.



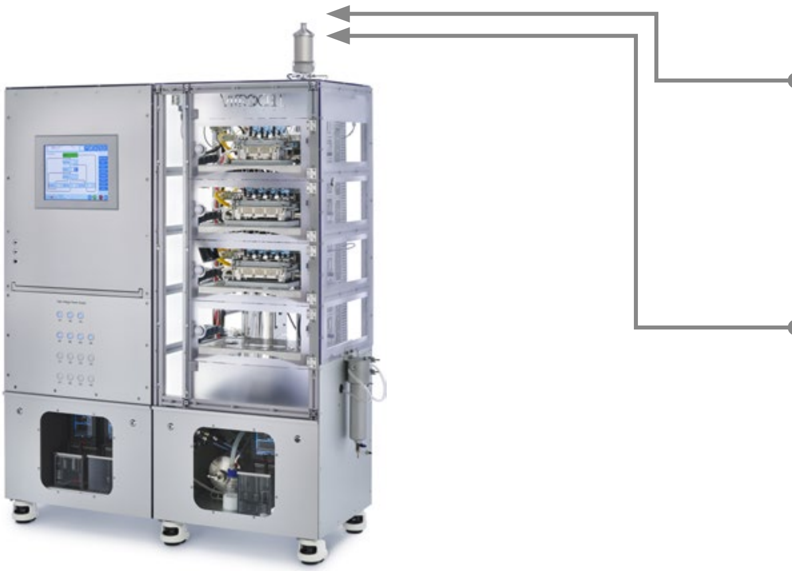


Application Areas



Application example for Continuous Flow Exposure

Automated Exposure Stations ▸▸▸ LONG EXPOSURE DURATIONS · 24 HOURS



- ○ Sampling from the environment
- ○ Operation in the lab with aerosol generators

Evaluation of complex mixtures including particles, for example from the environment or combustion processes.

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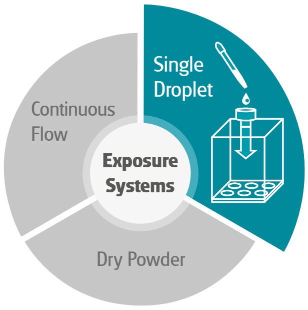
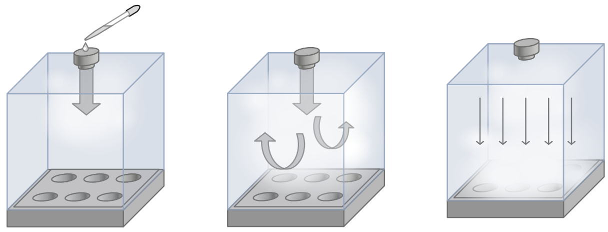
Exposure Principle 2:
Single Droplet Sedimentation (Cloud Exposure)



Single Droplet Sedimenation systems are specifically designed for dose-controlled and spatially uniform deposition of liquid aerosols on cells. Test substances are chemicals or particles brought into suspension with e.g. PBS.



Phase 1
Emission of Cloud

Phase 2
Homogeneous Mixing

Phase 3
Gravitational Settling

Application Areas

Application Example for Cloud Exposure

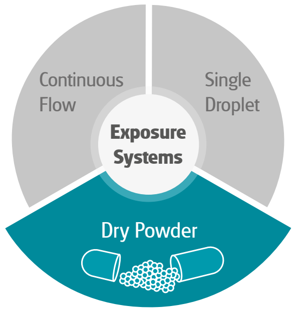
VITROCELL Cloud Alpha 12 ▸▸▸ 6–7 min. | 200 µl | 1 doses @ 9 rep. | 1 control @ 3 rep. | 12-/24-well | sQCM 12 optional

Easy-to-use system for liquid aerosols featuring a separate chamber for sham exposure.

- **Precise Dosing for Liquid Aerosols**
  Ideal for small quantities of liquid aerosols, ensuring accurate dosing and exposure.
- **Efficient Lab Operation**
  Works seamlessly with a nebulizer for efficient aerosol generation and delivery.
- **Integrated Heating System**
  Features an integrated heating system to maintain optimal aerosol conditions.
- **User-Friendly Design**
  Designed for ease of use, allowing smooth operation and minimal training requirements.

The optional sQCM 12 microbalance

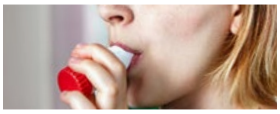
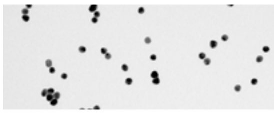
Exposure Principle 3 : Dry Powder Exposure



VITROCELL Dry Powder Exposure systems are specially designed for aerosolization of smallest quantities of dry powders.

This method is well suited for scarce and very expensive materials, such as new drug candidates or particle samples from the environment.

Application Areas


Application Example for Dry Powder Exposure

VITROCELL PowderX ▸▸▸ 1–100 mg | 1 doses @ 4 repl. | 12-/24-well

- **Precise Dosing for Small Quantities**
  Designed to handle the smallest quantities of dry powders with high precision.
- **Standalone Operation**
  Operates seamlessly in the lab without the need for an additional aerosol generator.
- **Customizable Sedimentation Time**
  Features programmable sedimentation time for tailored experimental conditions.
- **Integrated Heating System**
  Includes an integrated heating system to maintain optimal exposure conditions.
- **User-Friendly Interface**
  Engineered for ease of use, ensuring smooth operation and minimal training requirements


Quick-lock loading system open (left). Sealed expansion chamber (right).

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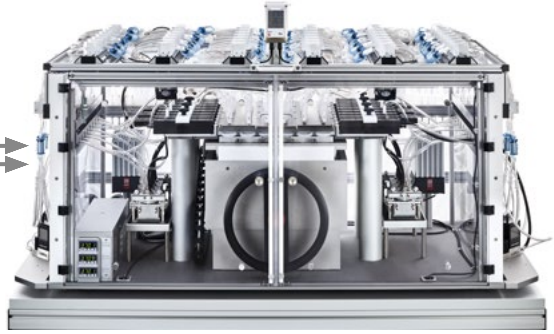
Continuous Flow Exposure: More Application Examples

VITROCELL 48 Climatic Chamber

▸▸▸ 7 doses @ 6 or 7 rep. | 1 control @ 6 or 7 rep. | 6-/12-/24-well, 35 mm petri dish

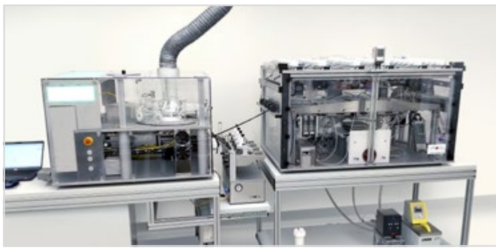


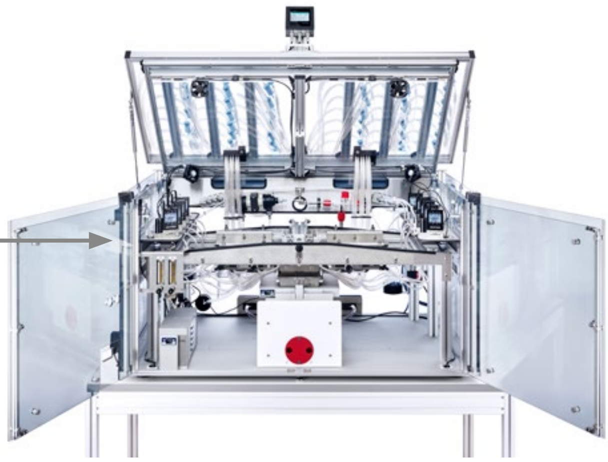
VITROCELL 48 Climatic Chamber with BioAerosol Generator (top) or Smoking Robot.

- Operation in the lab with a wide range of aerosol generators
- Climatic Chamber for best humdity level
- Condensation-free operation
- Integrated dynamic dilution system
- Dosimetry in 6th or 7th module position (PLUS version)

VITROCELL 24/48 Climatic Chamber

▸▸▸ 7 doses @ 6 or 7 rep. | 1 control @ 6 or 7 rep. | 24-well





VITROCELL 24/48 Climatic Chamber connected to VC 10 S-TYPE Smoking Robot

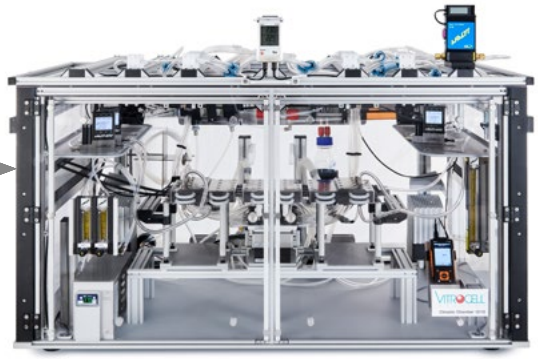
- Operation in the lab with a wide range of aerosol generators
- Climatic Chamber for best humdity level
- Condensation-free operation
- Integrated dynamic dilution system
- Dosimetry in 7th module position (PLUS version)

VITROCELL® SYSTEMS

Continuous Flow Exposure: More Application Examples

VITROCELL 12/12 ▸▸▸ 3 doses @ 3 or 4 rep. | 1 control @ 3 or 4 rep. | 12-/24-well

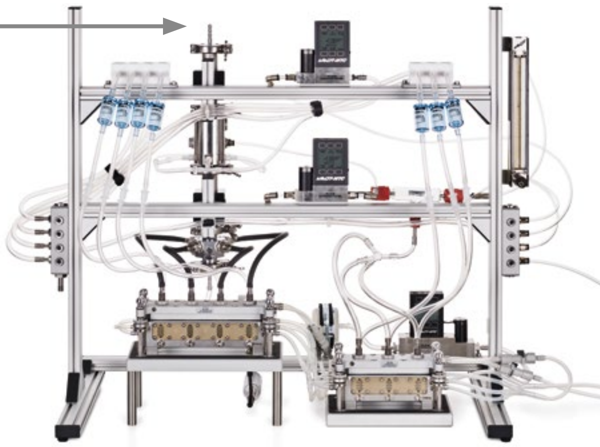
VITROCELL VC 1 S-TYPE Smoking Machine (top) connected to VC 12/12



- Operation in the lab with a wide range of aerosol generators
- Integrated dynamic dilution system

VITROCELL 6 Module Series ▸▸▸ 1 dose @ 4 rep. | 1 control @ 4 rep. | 6-/12-/24-well, 35 mm petri dish

VITROCELL BioAerosol Generator (top) and optional Climatic Chamber for VC 6 Module Series.



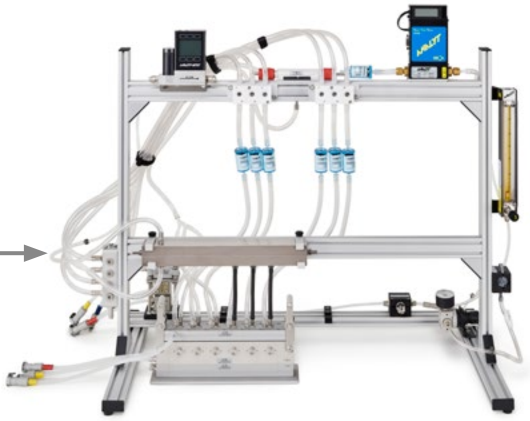
- Operation in the lab with aerosol generators
- Isokinetic distribution and dilution system
- Dosimetry in 4th module position

Continuous Flow Exposure: More Application Examples

VITROCELL 12/6

▸▸▸ 1 dose @ 3 rep. | 1 control @ 3 rep. | 12-/24-well

VITROCELL VC 1 Smoking Machine.



- Operation in the lab with a wide range of aerosol generators
- Dynamic dilution system
- Optional dosimetry module

VITROCELL 96

▸▸▸ 11 doses @ 9 rep. | 1 control @ 8 rep. | 96-well HTS plates

VITROCELL 96 with BioAerosol Generator (top) or Smoking Robot VC 10 S-TYPE (bottom).

- High throughput operation with HTS plates
- Operation in the lab with aerosol generators
- Dynamic dilution systems

Continuous Flow Exposure: Gas Supply

VITROCELL Gas Supply Systems

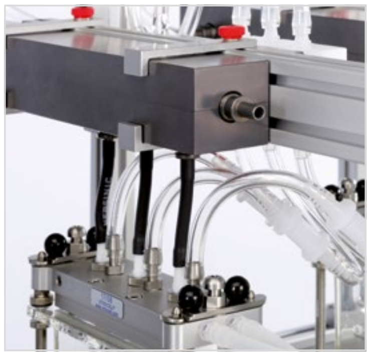
▸▸▸ Gases / Gas Mixtures

Sampling bag connected to module

Gases and mixtures in various concentrations and specifications can be purchased from gas supply companies. The cylinders must have pressure and flow regulators.

A sampling bag can be easily and directly connected to the module using the VITROCELL SPIDER (left). The bag can be filled from various sources.

With the VITROCELL Dynamic Gas Mixing System (right), it is possible to generate different dilutions of the test gas or gas mixture.



Dynamic Gas Mixing System

VITROCELL Spiking System

▸▸▸ Production of VOC / Gas Mixtures

The VITROCELL Spiking System (VSS) has been specifically designed to provide optimal results when exposing gas mixtures from solvents, gases and vapors.

It is the perfect solution when the required concentrations are not available in cylinders. The gas mixture is produced dynamically by means of a digital syringe pump allowing injections of less than 0.1 µl with high accuracy. The component is introduced into a zero gas.

Syringe drive

Continuous Flow Exposure: Aerosol Generators

VITROCELL 4-Jet BioAerosol Generator

▸▸▸ Liquid aerosols

The VITROCELL 4-Jet BioAerosol Generator has been specifically developed and engineered for applications where the test substance must be dosed in smallest quantities. This is performed using a peristaltic pump.

It works at low air flows of e. g. 0.4–4 l/min. and has a small dead space. The aerosol concentration can be adjusted by either adjusting the liquid flow rate, changing the air flow rate or by adding the integrated dilution system.

VITROCELL VRBG Generator

▸▸▸ Bulk powder aerosols

The VITROCELL VRBG aerosol generator has been specifically designed and engineered for the constant, continuous and reproducible generation of polydisperse solid aerosols from bulk powder material.

Connection to Exposure Modules via Isokinetic Sampling System

VITROCELL Abrasive Dust Generator

▸▸▸ Dust

The VITROCELL Abrasive Dust Generator generates dust particles which occur in grinding, cutting or other abrasive processes.

Aerosols containing particles from the following materials can be produced to evaluate their impact on human health:

- Synthetic materials
- Metals
- Ceramics
- Glass-fiber reinforced plastics
- Carbon-fiber reinforced plastics

Cloud Exposure: More Application Examples

VITROCELL Cloud Alpha 6

▸▸▸ 6–7 min. | 200 µl | 1 doses @ 6 repl. | 6-/12-/24-well | QCM 6 optional

Easy-to-use system for liquid aerosols featuring a wide range of insert sizes.

○ For small quantities of liquid aerosols
○ Operation in the lab with nebulizer
○ Integrated heating system
○ Easy to use

Optional QCM 6 microbalance

VITROCELL Cloud Alpha MAX

▸▸▸ 2–3 min. | 10–30 µl | 2 doses @ 3 repl. | 6-/12-/24-well

Easy-to-use system for liquid aerosols featuring a high deposition efficiency at very small test volumes.

○ For small quantities of liquid aerosols
○ Operation in the lab with nebulizer
○ Integrated heating system
○ Easy to use

Optional QCM 6 microbalance

VITROCELL Cloud Alpha MOVE

▸▸▸ 6–7 min. | 200 µl | 6 doses @ 4 repl. | 24-well

Easy-to-use system for liquid aerosols featuring the possibility for sequential exposure.

○ For small quantities of liquid aerosols
○ Operation in the lab with nebulizer
○ Integrated heating system
○ Easy to use

Sequential row-by-row exposure

Dosimetry for Exposure Systems

VITROCELL QCM 6

▸▸▸ 6-well dosimetry

Can be fitted in all VITROCELL installations. It is capable of measuring the deposited mass in the module at a resolution of 10 ng/cm^2 per second and is optimal for dose-response measurement.

Mounted QCM 6 microbalance and integrated in VITROCELL AMES 4

VITROCELL sQCM 12

▸▸▸ 12-well dosimetry

Simplifies the usage of conventional Quartz Crystal Microbalances suitable for VITROCELL 12 modules

- Online measurement of particle dose in ng/cm^2
- User-friendly mounting
- Supplied as turnkey system

VITROCELL Photometer 2.0

▸▸▸ Particle concentration

Enables online measurements of particle concentrations at the inlets and/or outlets of the aerosol exposure top. It is capable of measuring inline at very low flow-rates (e. g. 5 ml/min.) without any particle losses. Comes with a control box for 4 Photometers and the VITROCELL Monitor Software.

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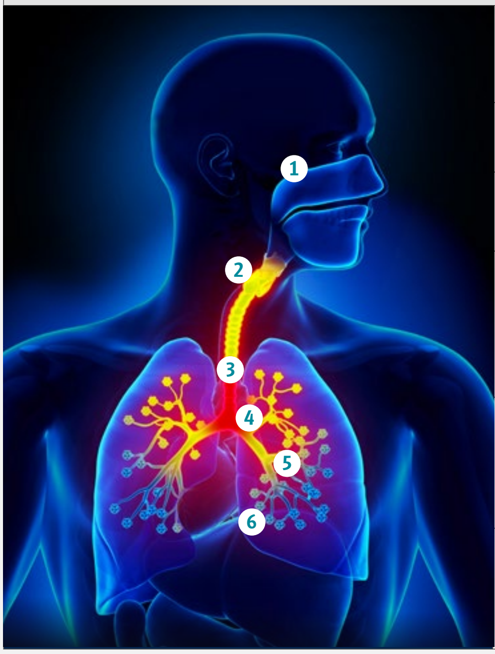
In vitro Testing for all Cell Types of the Respiratory Tract



Anatomy	Cell types	Function
1 Nose, mouth, esophagus	Ciliated cells, Non ciliated cells (Globet/Mucous/Serous/Brush/Endocrina/Basal/Intermediate cells)	Air conditioning, Temperature and humidity, Cleaning, Fast particle clearance, Air conduction
2 Trachea		
3 Main bronchi/Bronchi		
4 Bronchioles/Terminal bronchioles	Respiratory epithelium (Ciliated/Non ciliated cells (Clara))	Air conditioning, Gas exchange, Slow particle clearance
5 Respiratory bronchioles	Respiratory epithelium (Secretory/Few ciliated cells)	
6 Alveolar ducts and sacs	Alveolar epithelial cells	Gas exchange, Very slow particle clearance

Table adapted from Encyclopaedia of Occupational Health and Safety

Application Areas

System	Continuous Flow (Modules VC 6/12/24/96)	Cloud Exposure	Dry Powder
Application area			
Engine emissions and combustion exhaust incl. Diesel	x		
Tobacco and electronic cigarettes	x		
Environmental atmospheres	x		
Indoor air atmospheres	x		
Gases and mixtures	x		
Pesticides	x	x	
Household and industrial chemicals	x	x	
Pharmaceutical liquid aerosols		x	
Pharmaceutical dry powders	(x)		x
Virus research		x	x
Nanoparticles	x	x	x
Cosmetics	x	x	x

x = well suited (x) = for larger quantities of material

In vitro Assay Guide Examples

Category	Module type	VITROCELL 6	VITROCELL 12	VITROCELL 24	VITROCELL AMES
	Number of inserts	3 to 56	3 to 12	3 to 48	3 to 56
	Insert type (size)	6-well	12-well	24-well	35 mm Petri Dish
	Culture media supply	Static	Continuous	Static	Static
Cytotoxicity	Number of viable cells	x	xx	xx	–
	LDH release	xx	xx	xx	–
	NRU uptake	x	xx	xx	–
	MTT	x	xx	xx	–
	XTT	x	xx	xx	–
	MTS	x	xx	xx	–
Proliferation	WST-1	x	xx	xx	–
	Protein level	x	xx	xx	–
Cellular stress	ATP	xx	x	x	–
	Cellular ATP/ADP ratio	xx	x	x	–
	GSH	xx	x	x	–
	GSSG	xx	x	x	–
	GSSG/GSH	xx	x	x	–
Oxidative stress	Lipid peroxidation (MDA test)	xx	x	x	–
Inflammation	Cytokines like IL8, IL6, IL12	x	xx	xx	–
Genotoxicity	Comet assay	x	xx	xx	–
	AMES/number of revertants	–	–	–	x
"omic" Technologies	ARN Sample for microarray	xx	–	–	–
	ARN Sample for QRT PCR	xx	–	–	–
Molecular Biology	Protein Sample for Western Blot	xx	–	–	–
Assays for Suspension Cells		–	–	–	x

Legend:
x = well suited
xx = particularly well suited

About VITROCELL®

VITROCELL exclusively concentrates on the developing, producing, installing, training and servicing of advanced *in vitro* exposure systems.

The VITROCELL Systems' team is driven by their vision for new in-vitro standards through state-of-the-art technology, highly qualified workmanship and absolute client dedication. VITROCELL has successfully collaborated with clients from leading research institutes, contract research organizations, regulatory authorities or industrial laboratories across the world. Working with our team experts, all modules have been tailored to create durable and complete turnkey-systems for ***in vitro*** inhalation toxicology. Gases, environmental atmospheres, nano particles and complex mixtures are analyzed on lung cells at the air/liquid interface using these systems. VITROCELL technologies are also applicable to solutions for skin research.

Over a decade of devotion to research in this specific field has given our team of design & precision manufacturing specialists the opportunity to mentor highly diversified and complex projects **from conception to completion**. We strive to become a constructive member of each research team, providing support when it is needed, advice when it is required and modules of the highest quality, which are even polished by hand before leaving here to be integrated into your workspace. Every piece of our German engineered equipment is manufactured to the highest of standards – yours.

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