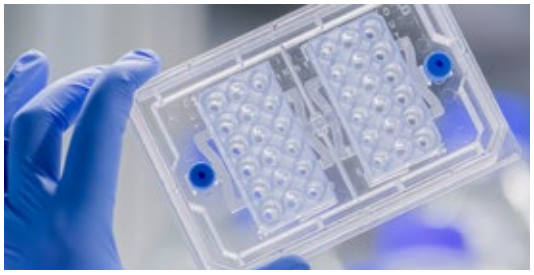
Advanced in vitro exposure systems



Product News

2022

Edition March 2022

VITROCELL® SYSTEMS

Combine breathing Lung-on-Chip with direct aerosol exposure

AlveoliX
In-vitro models inspired by nature

VITROCELL® Cloud α AX12

Aerosol exposure for breathing AX Lung-on-Chip

Vitrocell® Cloud Alpha AX12 – developed in close cooperation with AlveoliX.

Chip-based exposure of cell cultures

The VITROCELL® Cloud Alpha AX12 is our newest innovation in the Cloud family and presents a great leap forward in automated exposure of cell cultures with breathing function. It combines highly efficient testing with ease of use. The development is based on the well-known and frequently published VITROCELL® Cloud formats (6-, 12-, 24- and 96-well). Its functionality enables fully automated processes with an all-in-one control unit. Everyday experiments at the Air/Liquid Interface have never been easier.

It is suitable for the nebulization of solutions and suspensions. Fields of application are, but are not limited to, screening of inhaled drugs and toxicity testing of inhaled substances such as chemicals, nanoparticles and airborne pathogens.

Air / Liquid Interface

In response to the scientific need to expose in physiologically relevant conditions, the VITROCELL® Cloud Alpha exposure device has been specifically designed to enable direct exposure of cells or tissue at the Air/Liquid Interface. Here, the cell cultures are not covered with media in contrast to submerged conditions, which cause an undesired interaction of the formerly airborne substances with the culture media.

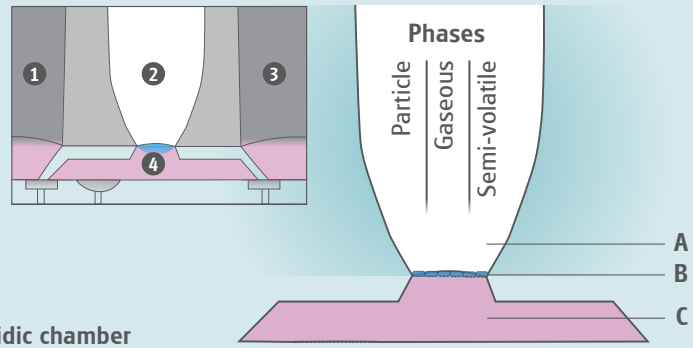
Cells cultivated on the membrane are exposed at the Air/Liquid Interface so that the test substances directly come in contact with the cells as aerosols. This approach allows for more in vivo like and lung-relevant cell response than if exposed to submerged conditions.

Air / Liquid Cultivation and Exposure

A Direct and controlled exposure of test atmosphere to cells

B Cells on ultrathin AX membrane

C Media below cells



(1) Inlet well, (2) Cell well, (3) Outlet well, (4) Fluidic chamber

VITROCELL® SYSTEMS

AX Lung-on-Chip System

The AX Lung-on-Chip System allows in vitro modeling in outmost physiological conditions by replicating the essential key features of the lung microenvironment.

- Ultrathin, porous, and elastic support for cell growth
- Breathing motion
- Air/Liquid Interface
- 3D tissues (multiple co-cultures)

The combination of the breathing-induced cyclic stretch and the optimized ultrathin cell culture substrate (AX membrane) preserves lung cells' functionality and phenotype. The technology provides answers to fundamental questions about lung biomechanics and cell biology. Furthermore, it is a powerful tool to recreate healthy, diseased, and personalized in vitro models, which can be implemented in drug development to test molecule efficacy and safety, and in toxicity assessment of e. g. pollutants, chemicals and consumer goods. This will hopefully lead to more animal free product development in the future.

The AX Lung-on-Chip System

AX Lung-on-Chip System components

Aside the AX12, the system is made up of three further components: two pneumatic controllers, AX Breather and AX Exchanger, and the AX Dock which is the interface between these two devices and the AX12.

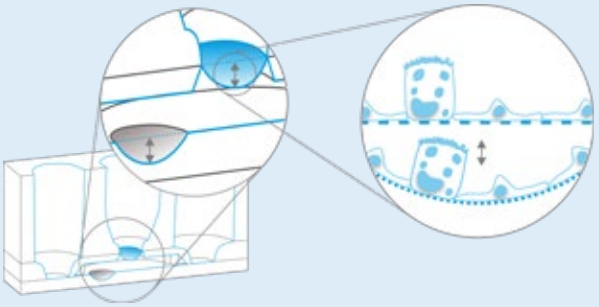
AX Breather The AX Breather controls the deflection of the micro-diaphragm inside the AX12, recreating the 3D cyclic breathing motion.

AX Exchanger The AX Exchanger enables a fluid flow for initial chip filling and medium exchange by pneumatically controlling the opening and closing of the valves inside the AX12.

AX Dock The AX Dock connects the AX12 with the AX Breather and the AX Exchanger creating an air-tight sealing for the pneumatic actuation.

AX12 The AX12 is the cell culture consumable and is based on a 96-well plate format. It consists of two chips supported by a plate and includes a total of 12 independent wells.

AlveoliX 3D Breathing concept



A nature-inspired concept is used to recreate the breathing motion. The ultrathin AX membrane (blue) is deflected by applying negative pressure inside the basal chip chamber through an integrated micro-diaphragm (grey).

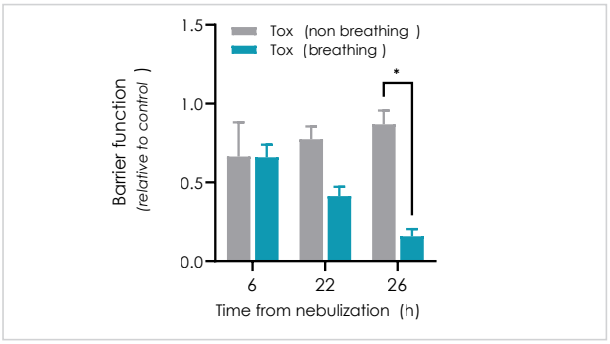
Aerosol Exposure and Lung-on-Chip

Ideal for small quantities of test substance

The VITROCELL® Cloud Alpha AX12 is designed for small nebulization volumes and has very high deposition efficiency. The recommended nebulization volume is 300 µl. Therefore, the device is particularly suitable for testing materials even when quantities are limited.

Dosimetry using Quartz Crystal Microbalance (QCM)

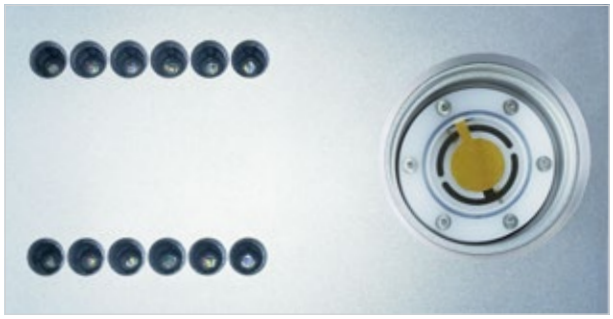
To assess the delivered dose, a QCM sensor is integrated into the Cloud Alpha AX12 exposure module. The microbalance can measure the deposited mass at a resolution of 10 ng/cm^2 per second. Results are reported online by the VITROCELL® Monitor software. Data is presented in graphs and stored in MS Excel®.



Time-course barrier function of lung epithelial cells upon nebulization with nanoparticles in breathing and non-breathing conditions. The delivered dose is equivalent to the lifetime exposure accumulated by a worker (45 years of work).

Key Features:

- Low nebulization volumes: 300 µl per exposure
- High deposition efficiency
- Easy handling with no external air-flow required
- Air/Liquid Interface exposure
- Breathing Lung-on-Chip system
- Porous membrane allowing cell-cell interaction
- Increased cell sensitivity in physiological conditions



The Cloud Alpha AX12 is equipped with a microbalance sensor.

Exposure combined with 3D breathing motion

Lung epithelial cells cultured on-chip exhibit robust barrier functionality in breathing conditions to the long term. When exposed to nebulized molecules at the Air/Liquid interface, cells demonstrated an increased sensitivity to airborne hazards, such as nanoparticles or known inhaled irritants, in breathing conditions. By simulating the in vivo situation, the Cloud Alpha AX12 in combination with the ^{AX}Lung-on-Chip enables more predictive toxicological assessment, inhalation-derived disease modeling, and potential evaluation of inhaled drugs.

Choice of four types of nebulizers

The system comes with a choice of 4 types of nebulizers having droplet MMAD ranges of 2.5 – 4.0 µm, 2.5 – 6.0 µm, 4.0 – 6.0 µm and 9.0 – 12.0 µm.

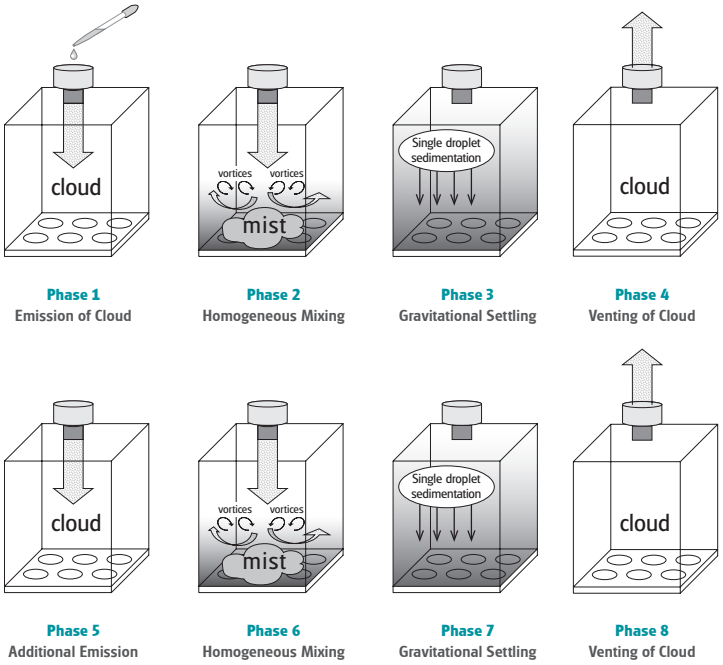
Cloud Alpha AX12 Base Module with AX12 and QCM

VITROCELL® SYSTEMS

VITROCELL® Cloud α PowerVent

Increase of nebulizations and evacuation of residual gaseous compounds

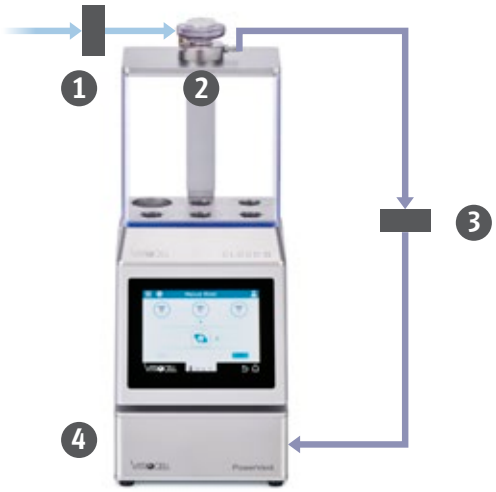
A typical Cloud exposure allows 3 consecutive nebulizations. The PowerVent option enables an increase of the dose by adding further nebulizations. After each nebulization the humidity is removed by a short venting period before starting the new one. The venting function can be edited in the software. The PowerVent unit is delivered ready-to-use with an integrated vacuum pump.



Phase 1 Emission of Cloud
Phase 2 Homogeneous Mixing
Phase 3 Gravitational Settling
Phase 4 Venting of Cloud
Phase 5 Additional Emission
Phase 6 Homogeneous Mixing
Phase 7 Gravitational Settling
Phase 8 Venting of Cloud

Vitrocell® Cloud Alpha 6 with PowerVent option.

PowerVent components



(1) HEPA filter for filtered air

(2) PowerVent adapter

(3) HEPA filter

(4) PowerVent Unit with vacuum pump

Key Features:

- Available for Cloud Alpha 6, 12 and 24
- Fast removal of residual gaseous compounds
- Allows >3 consecutive nebulizations
- Integrated vacuum pump
- Function can be edited in the software

VITROCELL® Cloud Advanced Nebulizer

For liquid droplet sizes 9–12 µm with diffusor

The VITROCELL® Cloud Advanced Nebulizer is enlarging the application areas of Cloud Exposure Systems. Whenever the suspended particles are larger than the mesh size of standard nebulizers (4.0 – 6.0 µm) this special type offers the possibility to produce an aerosol containing particles in the range of 9.0 – 12.0 µm.

Application Areas

- Pharmaceutical industry: formulations for nasal sprays often have larger particles sizes.
- Environmental research: on several projects PM 10 needs to be tested.
- Chemical Industries: certain chemicals need to be diluted substantially with PBS in order to make them work with the standard nebulizer. Here the VITROCELL® Cloud Advanced Nebulizer offers the possibility to generate an aerosol with no or less dilution.

Cloud Diffusor

The patented diffusor ensures a homogeneous distribution of even the larger droplet sizes in the Cloud Exposure Chamber. In order to avoid effects from larger droplet formations it has an integrated drain channel.

VITROCELL® Cloud Alpha with Cloud Advanced Nebulizer

Advanced Nebulizer

Diffusor

Nebulizer Controller

Flow Controller

VITROCELL® SYSTEMS

VITROCELL® S·QCM

Improved Sensor for High Precision Real-Time Dose Monitoring

The VITROCELL® sQCM 12 is the next step in the evolution of dosimetry methods in cell culture exposure systems. It simplifies the usage of conventional Quartz Crystal Microbalances suitable for VITROCELL® 12 modules while maintaining the working principle, precision and accuracy of the balances you're used to.

We have redesigned the entire sensor from scratch, enabling not only extremely high stability and exact measurements, but also eliminating the need for tools during service and cleaning for maximum user-friendliness.

sQCM mounted in VITROCELL® Cloud Alpha 12 module (left) and the new designed oscillator (right).

Performance, simplified

This novel solution minimizes the time you have to spend to perform cleaning and crystal exchange: it now only takes a mere minute. Eliminating the need for screwdrivers, our new design uses a bayonet catch to connect the individual sensor parts.

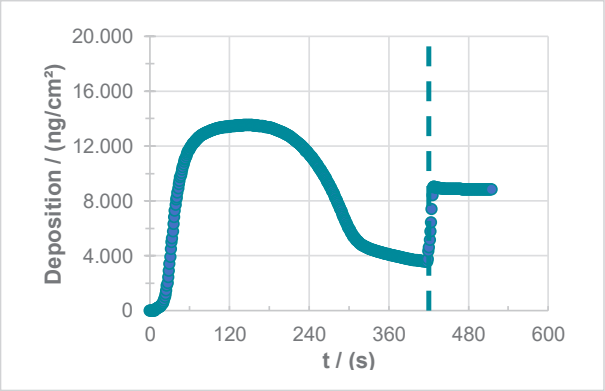
In Continuos Flow Systems, results are seen online, enabling you to measure cumulated depositions starting from 170 ng/cm² reliably. In Cloud systems, the sQCM 12 provides the additional benefit of real-time control over the process and exact readings after removal of humidity (dotted line on the right).

Wide Compatibilty

The innovative sensor design is fully compatible with any VITROCELL® module for 12-well sized inserts, be it Cloud, Cloud Alpha, Continuous Flow or any other VITROCELL® exposure system for this insert size.

Use Case

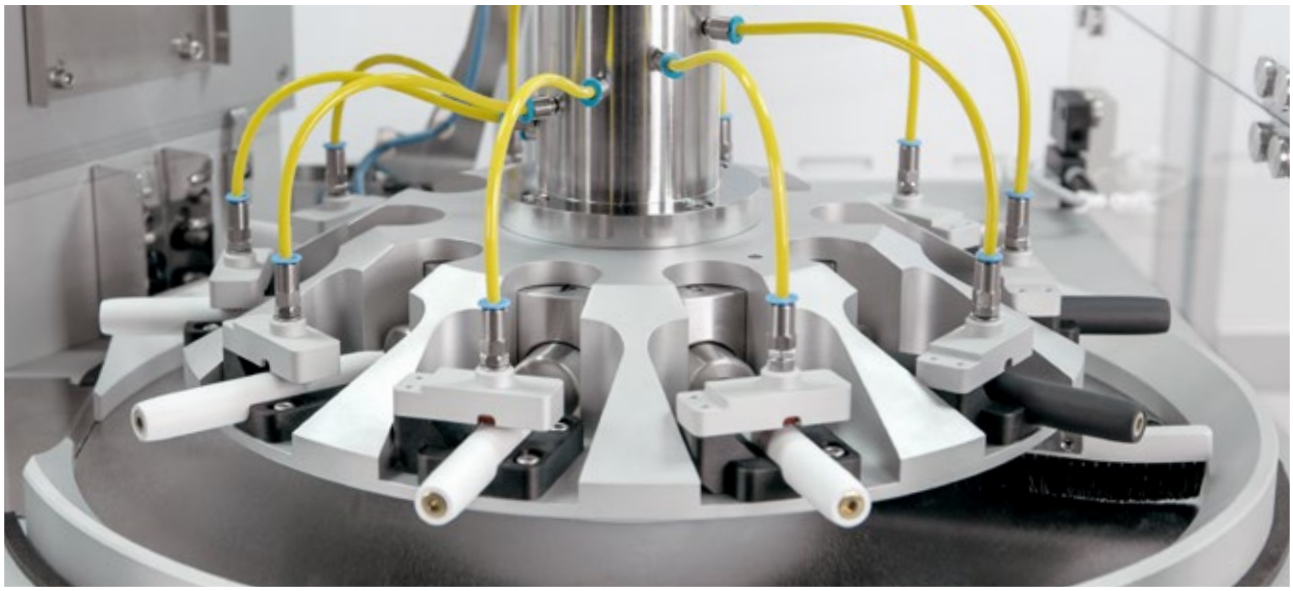
Thanks to the wide compatibility of the sQCM 12 sensor, it is ideal for the validation of the mass deposition of exposure substances, either during or after an experiment. Its broad measuring range and shape reminiscent of a cell-culture insert make it a convenient aid in acquiring single exposure doses or complete dose-response curves.



VITROCELL® Cloud Alpha 12 – Exposure of 0.2 mL 0.015 mg/mL Fluorescein and 9.54 mg/mL KCl

VC 10 S-TYPE Heat-and-Turn for Heat-not-Burn

For automated and continuous puffing of Heated Tobacco Products



Up to 10 devices can be installed on the support rim with individual button actuators.

Heated Tobacco Products require a button-activated pre-heating of the tobacco sticks prior to the smoking experience. During a smoking machine operation the pre-heating activation is either performed by the operator or – for improved handling and reproducibility – by automated button actuators.

The system is available for all commercial HTP devices.

Heat-and-Turn option for rotary Smoking Machine VC 10 S-TYPE

The heat-and-turn feature enables the VITROCELL® Vapestarter button actuator function for all 10 ports of the VC 10 S-TYPE Robot. Now continuous smoking and selective guidance of the aerosol to max. 6 exhaust lines are possible.

Key Features:

- Automated device activation
- Suitable for all commercial HTP devices
- Continuous puffing for up to 1 hour according to ISO and custom regimes
- Puffing to 1, 2, 3 or 4 exhaust lines (6 with triple piston drive)
- Time-saving, automated process
- Compatible with all VITROCELL® Exposure Systems

VITROCELL® SYSTEMS

VITROCELL® Smoking Machine VC 1 2.0

Manual smoking machine with high tech features

Options for e-cigarettes

- Square puff profiles
- Higher puff volumes
- Button actuator
- Heating option

The VC 1 smoking machine is used for a controlled aerosol generation of combustion cigarettes as well as of next generation devices such as Heated Tobacco Products (HTP) and electronic nicotine delivery systems (ENDS). Special attention was given to guarantee very flexible programming of the smoking parameters. The properties of the aerosol are maintained due to small dead volumes of the system. The requirements of all relevant ISO standards are met.

Fast and uncomplicated cleaning can be performed after each experiment or in case of a product change. The pump cylinder is easily dismantled, cleaned and remounted within a few minutes. The aerosol does not come into contact with the valve system, resulting in easy cleaning and increased reliability. An open design allows for uncomplicated installation of additional testing equipment, such as particle or gas analysers. All parameters of the smoking regime are freely programmable for puff volume, puff duration, puff frequency and exhaust duration.

Key features:

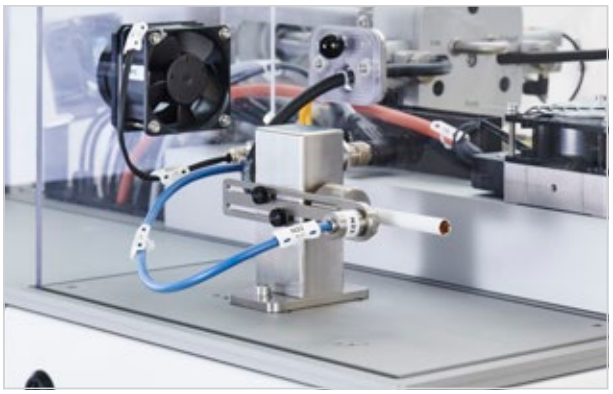
- Versatile platform concept for all types of test articles
- Requirements as of all relevant ISO standards are met
- Integrated automatic button actuation for ENDS and HTP's
- Fast cleaning
- Durable and easy to operate

Top: The Smoking Machine VC 1 is delivered turn-key with a laptop and modern HMI interface

Below: The platform enables easy access to all components. Picture shows the integrated heating system.

Versatility for all types of test articles

No matter which type of product: The VC 1 offers a platform for reliable smoking or vaping to all established standards. Easy cleaning and fast interchange of holders and actuators make the machine a versatile solution.



Combustion cigarettes

Draw actuated e-cigarettes

Button actuated e-cigarettes

Heated Tobacco Products (HTP)

VITROCELL® Holder System for e-cigarettes

New designs of ENDS (Electronic Nicotine Delivery Systems) lead to a large variety of different shapes making the insertion into conventional holders with labyrinth seals impossible.

VITROCELL® has developed holder systems which are flexible to adjust to different shapes. They are compatible with all VITROCELL® Smoking Machines & Robots.

Holder systems for JUUL (left) and Vaporesso Renova Zero (right)

VITROCELL® SYSTEMS

VITROCELL® Photometer 2.0

Online measurement of particle concentrations

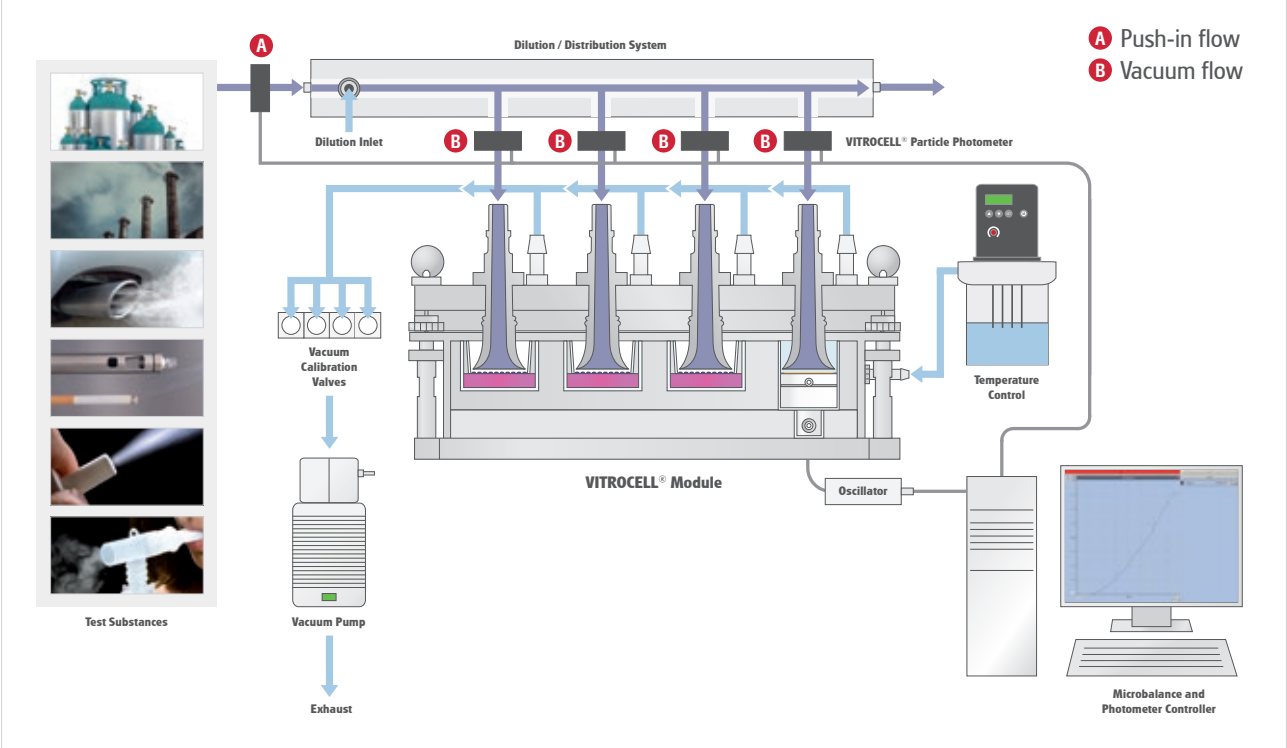
VITROCELL® Photometers are specifically designed and developed to enable online measurements of particle concentrations. The working principe is light-scattering. They may be placed inline at various locations of the exposure system without particles losses – even at low flow rates of e.g. 5 ml/min. The compact size of a mere 62 mm in diameter makes it fit almost anywhere.

Operation Modes – Easy Cleaning

The improved design enables an operation with a vacuum-generated or push-in flow. Examples for a vacuum flow are locations at the dilution system or inlet of the exposure modules. The push-in flow can be a measurement at the exit of an aerosol generator or smoking machine. The aerosol path can be easily cleaned with a soft pipe cleaner and Ethanol.

Sensitivity Ranges

The Photometer 2.0 is available in 2 base sensitivities: **HS** (high sensitivity) and **LS** (low sensitivity). Within the given base sensitivity a further range adjustment can take place via switch in 4 levels.



Photometer locations in the exposure system

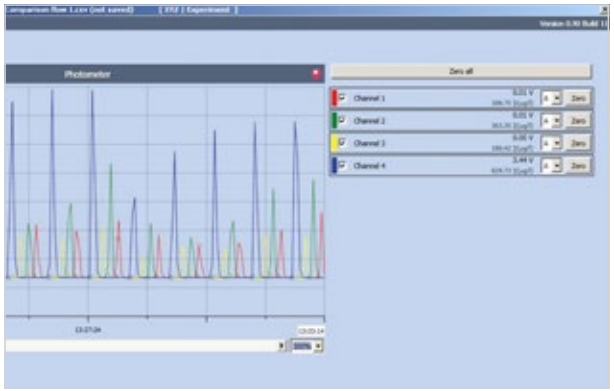
VITROCELL® Photometer Controller connects Photometers and Monitor Software.

Photometer Control Box and Software

The photometers are supplied with a control box for 4 Photometers and the VITROCELL® Monitor Software for convenient read-outs. The software features an area-under-curve function for easy determination of the total particle exposure. A calibration factor function enables a mass calculation per time units.

Monitor Software

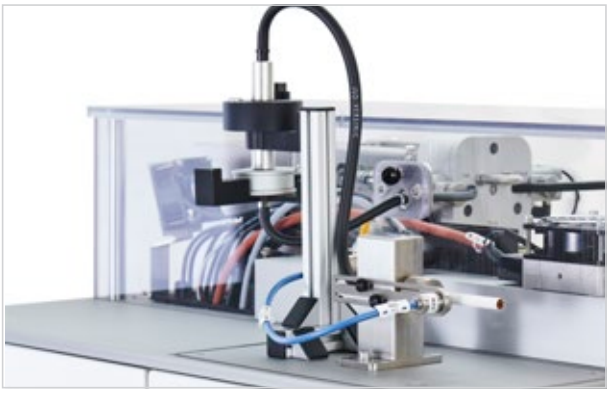
The VITROCELL® Monitor software enables data for max. 9 photometers to be presented online, including an area under curve calculation. The data is logged into a .csv file which can be opened in Excel®.



The VITROCELL® Monitor software is able to display the data from several Photometers at the same time.

Example Application – VC 1 Smoking Machine

The Photometer can be connected to a VC 1 Smoking Machine. It is monitoring the aerosol concentration puff-by-puff. TPM for chemical analysis is collected on a 44 mm Cambridge filter pad.



VITROCELL® Photometer connected to a VC 1 Smoking Machine.

Key Features:

- Inline measurement with online read-out
- No losses of mass
- Extremely small (62 mm diameter)
- Easy cleaning of aerosol path
- 2 base sensitivities with fine adjustments in 4 levels
- Push-in or vacuum flow operation

VITROCELL® SYSTEMS

VITROCELL® Remote Assist Support

Let us lend you a helping hand via HoloLens

VITROCELL *in vitro* exposure systems are specifically manufactured according to customer specifications. Our customers in the field of research & development typically have very complex requirements for the system. This is why a VITROCELL technician is required to carry out product training as well as service & support.

We strive to provide rapid responses and problem-solving for VITROCELL users all over the world.

Live Assistance with Augmented Reality

Augmented reality greatly facilitates this process. For VITROCELL we rely on the HoloLens 2 from Microsoft. It allows our support team to provide precise guidance in real time. The user's field of vision is transmitted to the technician's monitor, which enables him to provide training on the system remotely or offer troubleshooting advice.

Augmented reality technology makes it possible to project holograms such as an arrow marker or data sheets into the customer's field of vision.

It is also possible to interact using speech and gestures. This practically eliminates the possibility of misunderstandings.

VITROCELL technicians can also deliver visual instructions via a live video chat with Microsoft Teams.

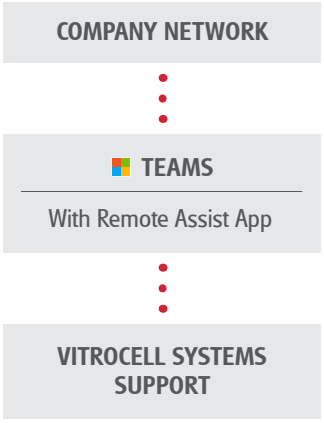
These are shown to the user as holograms in real time with the Microsoft HoloLens.

Microsoft HoloLens

The Microsoft HoloLens is a stand-alone, holographic computer. It enables users to see holograms, i.e. digital content, in their real field of vision. These three-dimensional graphics or images are projected onto the projection glass of the HoloLens. They are therefore only visible to the user and create a realistic image. Sensors and special systems such as eye, finger and hand tracking enable users to interact with the holograms. The microphone and speakers also allow for verbal communication. As the flagship device in the intelligent edge sector, HoloLens 2 works almost completely trouble-free even without a reliable internet connection.

Microsoft Dynamics 365 Remote Assist

The HoloLens offers an almost unlimited number of possible applications. In addition to decentralized training solutions as well as trade fair and sales experiences, location-independent support is one of the most popular applications. The Remote Assist application from Microsoft makes this possible. Due to the comfortability of the HoloLens that is leaving both hands free, the user is able to carry out the required operations easily and efficiently. This eliminates the need for on-site visits, even in the case of complex systems, which saves time and facilitates rapid assistance.



How the Microsoft HoloLens connects to the VITROCELL® Support team

The Microsoft HoloLens enables the user to use both hands to perform the required operations, even on complex systems.

Key Features:

- Hands-free audio and video calls
- 2-way freehand drawings and arrows can be drawn into the real environment
- Chat/instant messages during calls
- Compatible with Microsoft Teams: Remote workers can make and receive calls using Teams Desktop or Teams Mobile
- OneDrive integration: Documents (PDF) and images (JPG, PNG, TIFF and BMP) can be displayed.
- Corporate level identity and security: AAD authentication and single sign-on
- Screen sharing: Experts can project their desktop screen onto HoloLens users' field of view

System requirements:

- The service is set up by VITROCELL as part of the Remote Assist Package.
- The customer requires a Wi-Fi internet connection
- If this is not possible, the transmission can take place via the mobile network

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.

For more information please scan the QR-Code:

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