In vitro inhalation research: Expert precision

TJI catches up with VITROCELL's Managing Director Tobias Krebs to learn about the company's new innovations, the importance of face-to-face customer interaction and the advantages of in vitro exposure systems.

We last spoke three years ago. What has been happening at VITROCELL since?
Since we last spoke, we've been delighted to resume visiting our customers and attending conferences, where we can once again meet face-to-face with the researchers working in our field. This has been an incredibly positive development for us. Within VITROCELL, we have honed our focus on several key areas. As a leading company in in vitro exposure systems, we've refined our product solutions along two dimensions. Firstly, we now offer devices capable of evaluating the full spectrum of aerosol categories. This includes:
Gases and Complex Mixtures: Such as those found in combustion, ENDS, and heated tobacco products.
Liquid Aerosols: Where chemicals and pharmaceutical compounds are aerosolized from a suspension.
Dry Powder Aerosols: Where minute quantities of the test substance can be exposed to cell cultures.
These advancements have expanded our applications into new areas of pharmaceutical and environmental health risk assessment.
Secondly, our product range is designed to meet the needs of both very small labs and large Contract Research Organizations (CROs), where systems with the highest throughput are required.
Additionally, we have developed and refined our tools for dosimetry. This is crucial in both research and regulatory work to ensure that applied doses are relevant to human exposure. Unfortunately, some publications neglect the importance of relevant dosimetry and use exposure methods that are not applicable to the human situation, which raises questions about their relevance for risk assessment. Addressing dosimetry correctly is essential, and our equipment is designed to accurately assess aerosols ▶

VITROCELL 96: High Throughput Exposure System for 96-well HTS Plates

Photos: VITROCELL

and complex mixtures, ensuring that our methods are both scientifically valid and relevant to human health assessments.

What have been the biggest challenges?

One of our biggest challenges has been developing a reliable method to aerosolize the smallest quantities of dry powders and ensure they deposit accurately on cell cultures. We now have a very reliable solution not only for exposing compounds from new drug candidates but also, for instance, moon dust. With new visionary space plans, the toxicological assessment of substances in space is becoming increasingly important.

Another significant challenge was creating exposure solutions for 96-well High Throughput Plates. With these plates, we can conduct experiments with 12 different concentrations across 8 replicates, resulting in a substantial amount of data from a single run.

We are also proud to have developed solutions to expose a lung-on-chip to all the aerosol types mentioned earlier. In close collaboration with our partner AlveoliX AG, we can now offer aerosol exposure to a breathing lung-on-chip at the human-relevant air-liquid interface. This method closely mimics the human situation by replicating the stretch of cells as it occurs in the human lung.

However, the biggest ongoing challenge is increasing regulatory acceptance of relevant in vitro exposure methods. Traditional methods still dominate the regulatory field, often requiring animal experiments. We need to question the relevance of results from animal exposures to humans. There is still much to be done before animal exposure tests are fully replaced by more relevant, state-of-the-art in vitro inhalation studies. In my opinion, far more effort should be directed towards the validation of new in vitro methods, all of which are currently available. This validation process will require oversight and funding from government research organizations, regulatory authorities, and industry stakeholders.

What have been the biggest successes?

Over the last three years, our customers have published an increasing number of excellent studies and research papers that describe their work with VITROCELL equipment. It's incredibly rewarding to see so many presentations and posters featuring our technology at relevant conferences.

On the technical side, our solutions, as previously mentioned, have been performing exceptionally well, which we consider a significant achievement. This success has also led to an influx of new customers from beyond the tobacco industry, including those in pharmaceutical and environmental research sectors.

Moreover, we've made significant advancements in simulating longer-term effects by

exposing cell cultures continuously for up to 72 hours in our new AirTox Monitor. This capability is crucial for environmental testing and could also be applied to Next Generation Products (NGPs). These long-term exposure features are vital for understanding chronic effects, making our equipment even more versatile and valuable for a wide range of applications.

The tobacco industry is constantly changing, how does VITROCELL keep up with new rules and regulations?

As an equipment manufacturer, we prioritize compliance with all relevant technical standards and maintain our ISO 9001 certification, which provides a solid foundation for adapting our processes to meet evolving requirements. This certification helps ensure that our quality management systems are robust and flexible enough to handle regulatory changes.

We stay informed about industry changes through continuous engagement with regulatory bodies, participation in industry forums, and collaboration with our customers. This proactive approach allows us to anticipate and prepare for new regulations before they come into effect.

In addition to technical compliance, we are committed to supporting our customers' needs in meeting regulatory requirements. For instance, we ensure our software is GLP-compliant and update it regularly.

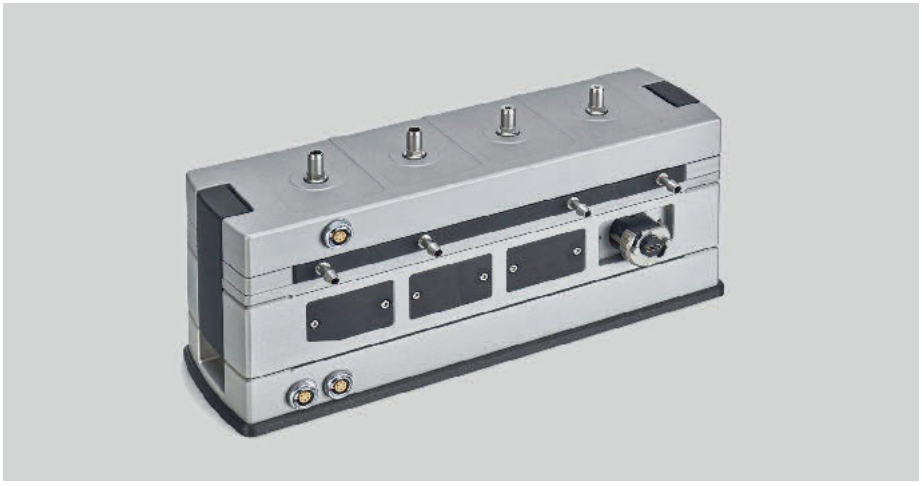
Furthermore, our participation in industry conferences and workshops allows us to stay ahead of trends and regulatory shifts. This engagement not only keeps us informed but also enables us to contribute to the development of best practices and potential new standards

In your opinion, is the tobacco industry becoming overregulated?

It's difficult to speak on behalf of our customers, but from a health risk assessment and consumer protection standpoint, regulation is definitely necessary. Without proper regulation, cases like EVALI, involving Vitamin E acetate, can happen again when unsafe and untested products are sold in the market.

However, the requirements in this regulatory process need to be clear and transparent. It's essential for regulators and the industry to establish clearly defined and validated methods. As mentioned earlier, new reliable in vitro methods already exist, and they should have a well-defined place in regulation. This would not only ensure safety but also streamline the regulatory process, making it more effective and efficient.

VITROCELL VC 10 S-TYPE: automated and continuous puff generation of Heated Tobacco Products



VITROCELL FLOW 4
Exposure module platform

Have you noticed a change in how your customers use your smoking machines? Are NGPs taking over from cigarettes?

The shift from combustion cigarettes to Next Generation Products (NGPs) has been a noticeable trend for many years. Today, our machines are designed to handle a wide range of products and devices, even the most "exotic" versions. However, a significant challenge persists: in smaller labs or universities, often home-made or low-budget solutions are used for research.

The aerosol for an in vitro test must be generated in a very precise manner, combined with reproducible dosimetry. Solutions that, for example, use vacuum pumps for aerosol generation do not provide the precision needed to advance the science in this field.

Ensuring accurate and consistent aerosol generation is crucial for reliable research outcomes, and this is where high-quality equipment like ours makes a significant difference.

What sets your smoking machines apart from the competition?

Our machines comply with all ISO standards and CORESTA recommended methods, similar to any other machines used in quality control. However, several key features set our machines apart:

Unfiltered Whole Aerosol Handling: Our machines are designed to work with unfiltered whole aerosol, which is then ▶

directed to the exposure systems. This capability requires robust heavy-duty drives and easy cleaning with fast access to all components, ensuring that valves are not in contact with the aerosol.

Specialized Software: Our software features are optimized specifically for conducting in vitro experiments. These features enhance the precision and efficiency of experimental procedures.

Advanced Capabilities: A prime example is our VC 10 S-TYPE Smoking Robot, which can handle 10 Heated Tobacco Products (HTP) devices for continuous aerosol generation. It can selectively guide the aerosol to up to 6 different exhaust lines, offering new possibilities in experimental design and execution.

These unique features ensure that our machines provide the reliability, precision, and versatility needed for advanced research and quality control in the field of aerosol exposure and in vitro testing.

Last time we spoke, you said you were launching around eight new products each year, is this still the case?

Yes, this is still the case. In 2023, we introduced seven new solutions, and we are on track to launch eight new products again this year. Our commitment to innovation remains strong, and we continue to develop and refine our offerings to meet the evolving needs of our customers and the industry.

Can you please tell us a bit about your new products?

Certainly. I provided some insights earlier, but I'd be happy to elaborate. Our new products are well-received across industry, research, and regulatory bodies. One of our primary focuses has been to make our systems easier to use, which is especially crucial in academic settings where there is a constant turnover of operators. When a super-user moves to another institute, rebuilding the know-how can be challenging. By enhancing the ease of use, we facilitate smoother handovers and more consistent use. To support this, we've expanded our service options with global training and refresher seminars.

Some of our latest developments include:

96-Well Exposure System: We have just completed testing our new 96-Well Exposure System for Combustion and Heated Tobacco Product (HTP) aerosols. A publication detailing this system will be released soon.

FLOW 4 Generation of Exposure Modules: On our path to advanced dosimetry, we have introduced the new FLOW 4 generation of exposure modules, which comes with the most comprehensive set of features to date, including increased ease of use. These modules are designed to simplify operation and maintenance, making them accessible even to users with less experience, thereby ensuring consistent performance and accurate results.

ESSENTIALS Line for Universities: For academic institutions, we introduced the ESSENTIALS line, which includes basic functionalities necessary for reliable in vitro exposure. This line is designed to meet the needs of educational and smaller research labs with straightforward, user-friendly equipment.

New Methods for Dosimetry and Process Control Sensors: We are also working on new methods for dosimetry and developing sensors for process control parameters, further enhancing the precision and reliability of our systems.

These advancements reflect our commitment to innovation and to meeting the evolving needs of our diverse customer base.

Are you working on anything new at the moment?

Innovation is a constant process for us at VITROCELL, and we are continually developing new products and solutions. Our commitment to advancing the field means that we always have several projects in the pipeline, aiming to address the evolving needs of our customers and the industry. We are excited to continue presenting new advancements that push the boundaries of in vitro exposure technology.

Will we be seeing VITROCELL at any trade fairs this year?

Yes, we have been very busy this year, attending six conferences already, including our User Group Meeting. You can catch us at EUROTOX in Copenhagen this September. Additionally, we are very much looking forward to participating in the CORESTA Congress in Edinburgh. These events are excellent opportunities for us to connect with industry peers, showcase our latest innovations, and engage with the research community.

What can visitors expect to see at your stand?

Visitors to our stand can expect to see our latest products and innovations in in vitro exposure technology. However, equally important to us is the opportunity to receive feedback and updates from our customers. We value these interactions as they help us understand our customers' needs and how we can continue to improve our solutions. We look forward to engaging with attendees, discussing their challenges, and exploring how our technology can support their research and regulatory requirements.

Finally, is there anything else you would like to share with TJI's readers?

I would like to thank TJI for giving us the opportunity to provide this update. Additionally, I wish to extend my gratitude to our customers for their fantastic cooperation and the many good ideas they have shared with us.

Interview: Tanya Wolf