Fraunhofer
ITEM

FRAUNHOFER INSTITUTE FOR TOXICOLOGY AND EXPERIMENTAL MEDICINE ITEM

ANNUAL REPORT 2017

FRAUNHOFER INSTITUTE FOR TOXICOLOGY AND EXPERIMENTAL MEDICINE ITEM

PERFORMANCE AND RESULTS

ANNUAL REPORT 2017

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ITEM, QUO VADIS? – INTERVIEW WITH THE INSTITUTE DIRECTOR

In 2017, Prof. Norbert Krug took over as Fraunhofer ITEM executive director from Prof. Uwe Heinrich, who had successfully managed the institute for 20 years. We are taking this opportunity to present you here with an interview with the institute director, in contrast to the traditional foreword you used to find on these pages in our previous annual reports.

Prof. Krug, you have contributed to shaping the Fraunhofer Institute in Hannover for 17 years already: In 2000, you became Division Director of Immunology, Allergology and Airway Research at Fraunhofer ITEM and thereafter played a leading role in setting up the institute's Department of Clinical Airway Research and eventually the Clinical Research Center Hannover – the CRC Hannover. You have been part of the institute management since 2008 and have now become executive director. Over the years, you have witnessed some truly significant changes – what do you think are the greatest challenges and opportunities for the institute?

During its over 35 years of existence, Fraunhofer ITEM has evolved from an institute with a focus on inhalation toxicological environmental research to an institute for medical translational research – with its three business units "Drug Development", "Chemical Safety and Assessment" and, since 2017, "Translational Biomedical Engineering".

Being an institution of the Fraunhofer-Gesellschaft, Europe's leading organization for applied research, our primary mission includes offering attractive R&D services tailored to market requirements. Markets, however, are subject to constant change – sometimes more and sometimes less pronounced. This means that we at Fraunhofer ITEM, offering research services to the public sector and to pharmaceutical, chemical, and biomedical engineering companies, are challenged as well to explore new topics, new fields of activity, to further enhance existing competencies or, if need be, realign these in anticipation of trends and developments. And this is exactly the challenge we will strive to meet in the years to come.

Perhaps you could be more specific – what will be the future research and development topics at Fraunhofer ITEM?

Well, digitalization will definitely be one of our focuses. We will enhance our activities in the fields of data analysis and bioinformatics, because we would like to push the creation of value from large quantities of data – catchphrase "big data" – both for drug development and for toxicological issues in chemical safety assessment.

In addition, we intend to further develop our capabilities in preclinical toxicology and pharmacology to position ourselves optimally for the relevant future topics of translational research, such as nanotoxicology, development of predictive human disease models, and development of advanced therapy medicinal products, ATMPs in brief. Furthermore, we will actively participate in developing the "toxicology of the 21st century", aiming to establish new assessment concepts for hazard and risk assessment of chemicals. These will involve cutting-edge, human-relevant in-vitro non-animal methods and in-silico computational technologies.

Another topic we will increasingly focus on is infections. Infectious diseases pose an increasing global threat, due to their rapid spread and the ever faster development of resistances to antibiotics. There is an urgent need for new therapies. At Fraunhofer ITEM, we will enhance research on infections and their treatment, with increasing use of cross-disciplinary approaches. Examples are the collaborative projects Phage4Cure and iCAIR. Phage4Cure is a project in which we collaborate with colleagues from Leibniz Institute DSMZ and Charité in Berlin to establish bacteriophages as an approved drug for treating bacterial infections. In the German-Australian research consortium iCAIR, we have teamed up with colleagues from the Hannover Medical School and Griffith University in Australia to develop new anti-infective drugs.

After this glance at the future, let us look back at the year 2017. What was at the focus of Fraunhofer ITEM in 2017?

Our focus in 2017 was on "networking" – in particular on networking with the adjacent Hannover Medical School, the Helmholtz Association, and universities. A recent example is the "proof-of-concept initiative". Through this initiative, the Helmholtz Association, Deutsche Hochschulmedizin (i. e. the peak organization of German university hospitals and medical schools) and the Fraunhofer-Gesellschaft want to work out strategies that will make it easier to overcome the biggest obstacle to developing new drugs, which is getting them from the laboratory into clinical trials. Upon a joint call, the initiative is funding projects in which the partners Fraunhofer, Helmholtz and Deutsche Hochschulmedizin are collaborating in the field of translational research. The pilot phase will be funded in equal parts by Fraunhofer and Helmholtz – with a total of twelve million euros over three years. The projects are intended to prepare a national "proof-of-concept platform" conceived by the German Federal Ministry of Education and Research within its Health Research Forum. More than 80 project proposals have been submitted – Fraunhofer ITEM is involved in 19 of these.

Furthermore, our network was strengthened in 2017 through the establishment of the Fraunhofer High-Performance Center Translational Biomedical Engineering, in particular with the Leibniz University of Hannover and the Hannover Medical School – regarding the latter by means of a concurrent professorship instituted together by the Hannover Medical School and Fraunhofer ITEM, connecting the research done in the clusters of excellence REBIRTH and Hearing4all in Hannover and in the Lower Saxony consortium "Biofabrication for NIFE" directly with the translation expertise of Fraunhofer ITEM. The aim is to bring medical devices from the lab into phase I of clinical development, a process the new EU-wide Medical Device Regulation in particular has made very difficult. The focus at present is on inhalers as smart drug devices and on implants such as cochlear implants.

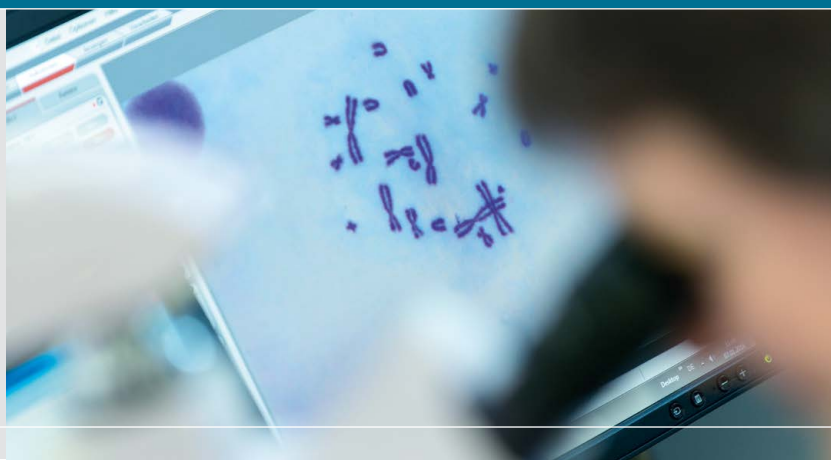
Networking is also performed within the Fraunhofer-Gesellschaft: by setting up collaborations of institutes with complementary fields of activity and by pooling the special expertise of institutes with similar thematic orientation. An example is the Fraunhofer Cluster of Excellence "ImmuVision". It unites the Fraunhofer Institutes IZI, IME, and ITEM in a single virtual institute where they all bring in their expertise to develop personalized medicines and therapies for disorders caused by malfunction of the immune system.

Prof. Krug, what is your personal wish for Fraunhofer ITEM?

My wish is to see Fraunhofer ITEM well positioned for the future – that we have anticipated the right impulses and trends and manage to translate these into successful developments that will eventually become products meeting market demands.

PROFILE OF THE INSTITUTE

Research at Fraunhofer ITEM is focused on human health – and this has been so for over 35 years. The emphasis is on two aspects: firstly, on protecting health from potentially harmful, in particular airborne substances, be they gases, aerosols, particles, fibers, or nanomaterials, and secondly, on investigating and developing diagnostic and therapeutic approaches in the field of inflammatory and allergic respiratory conditions, both at the preclinical and clinical levels. Complementing these thematic focuses, Fraunhofer ITEM also engages in other subject areas, such as development and manufacturing of biopharmaceuticals, tumor therapy, and translational biomedical engineering.



Health protection

Health protection includes environmental, occupational, and consumer protection. Fraunhofer ITEM supports industry and public authorities in the early identification and prevention of health hazards from new products and processes. In this context, Fraunhofer ITEM scientists investigate novel products and processes whose potential health hazards are as yet unknown, such as different nanomaterials. They evaluate the human exposure situation and develop suggestions on how to reduce or eliminate these potential hazards. For the experimental part of risk assessment, Fraunhofer ITEM has at its disposal the necessary know-how and toxicological test methods, in particular in the field of inhalation toxicology. For the required tests, complex atmospheres and test aerosols can be generated at laboratory scale and exposure scenarios can be reproduced for in-vitro or in-vivo studies. Special computerized mathematical exposure models are also developed and used for this purpose.

21st-century assessment of chemical safety

Fraunhofer ITEM scientists perform exposure and risk assessment of chemicals on behalf of clients, based on their own experimental studies, literature searches, and data provided by the client. Integrated approaches to testing and assessment of chemicals are becoming more and more important in this context. This means that the scientists are breaking new paths towards mechanism-based toxicological assessment. In this paradigm shift in toxicological assessment, in-vitro methods – human-relevant methods in particular – and in-silico methods are playing a crucial role. In-silico approaches today are no longer limited to deriving the toxicity of a substance from its structure, but also include toxicity and effect profiles.

Drug development

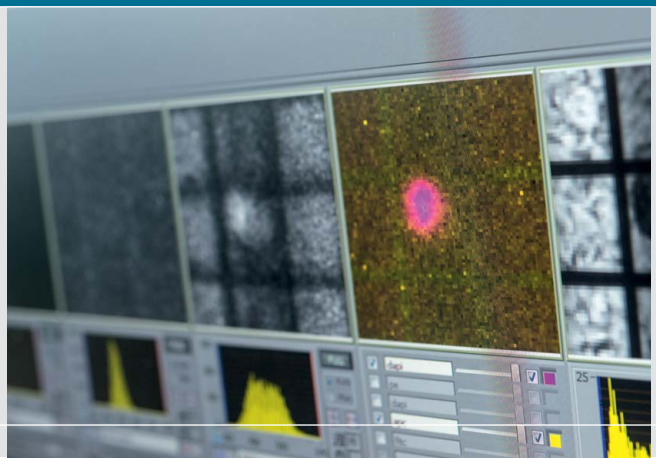
Before a drug candidate can reach final approval for commercialization, it has to go through a multistage development process that takes several years. Research at Fraunhofer ITEM is geared to this development sequence, and we accompany clients through its different phases. As researchers in translational medicine, working at the interface of basic research, clinical application, and drug regulatory requirements, we aim to translate scientific results into benefits for patients.

Biopharmaceutical manufacturing: from cell line to investigational medicinal product

In the institute's facilities in Braunschweig, Fraunhofer ITEM scientists develop manufacturing processes for novel biopharmaceutical agents: from the development of recombinant production cell lines via the manufacturing of master and working cell banks, bioprocess development and scale-up, to the manufacturing of pilot batches of the novel biopharmaceutical agent and sterile fill and finish of investigational medicinal products in the form of infusion solutions or in vials or ampoules – in compliance with GMP guidelines.

Preclinical testing of candidate drugs

The institute offers a broad range of efficacy and drug safety studies and makes use of a variety of in-vitro test systems and models of inflammation, asthma, lung infection, and pulmonary fibrosis. The use of human tissue in in-vitro and ex-vivo test systems in particular allows Fraunhofer ITEM scientists to obtain human data at an early stage already, data of pivotal importance above all in the testing of biopharmaceuticals.



Throughout the entire research and development process, Fraunhofer ITEM scientists are keeping an eye on the ethical principle of the "3 Rs" – they are well aware of their great responsibility for the well-being of the animals they use in their experiments. The three Rs stand for Replacement – the use of alternative methods that avoid or replace the use of animals –, Reduction – strategies that will result in fewer animals being used – and Refinement – modification of husbandry or experimental procedures to minimize pain and distress. Research at Fraunhofer ITEM is geared to using less animals to answer research questions, to consistently improving research methods, and to replacing animal experiments by alternative methods whenever possible. Fraunhofer ITEM scientists, therefore, participate in different projects aimed at developing non-animal methods – in vitro, ex vivo, and in-silico – and at validating these as test systems for drug safety assessment and registration.

Clinical trials for efficacy and tolerability testing of novel drugs

Efficacy and tolerability testing of novel drugs in humans is the critical step in medical translational research. Fraunhofer ITEM offers clinical trials to this end – in particular for the therapeutic areas allergy, asthma, COPD, and pulmonary fibrosis. The focus is on proof-of-concept studies in compliance with GCP guidelines, managed by highly qualified physicians. The CRC Hannover (Clinical Research Center Hannover) with its state-of-the-art infrastructure offers optimal conditions for performing this step.

With the Fraunhofer Challenge Chambers, special facilities for controlled challenge are available. The efficacy of novel medications to treat allergies, asthma, or airway inflammation can be tested here under controlled conditions. At the end of 2017, a sleep laboratory was set up in the phase-I unit of the CRC Hannover. Fraunhofer ITEM thereby has extended its diagnostic possibilities in clinical research.

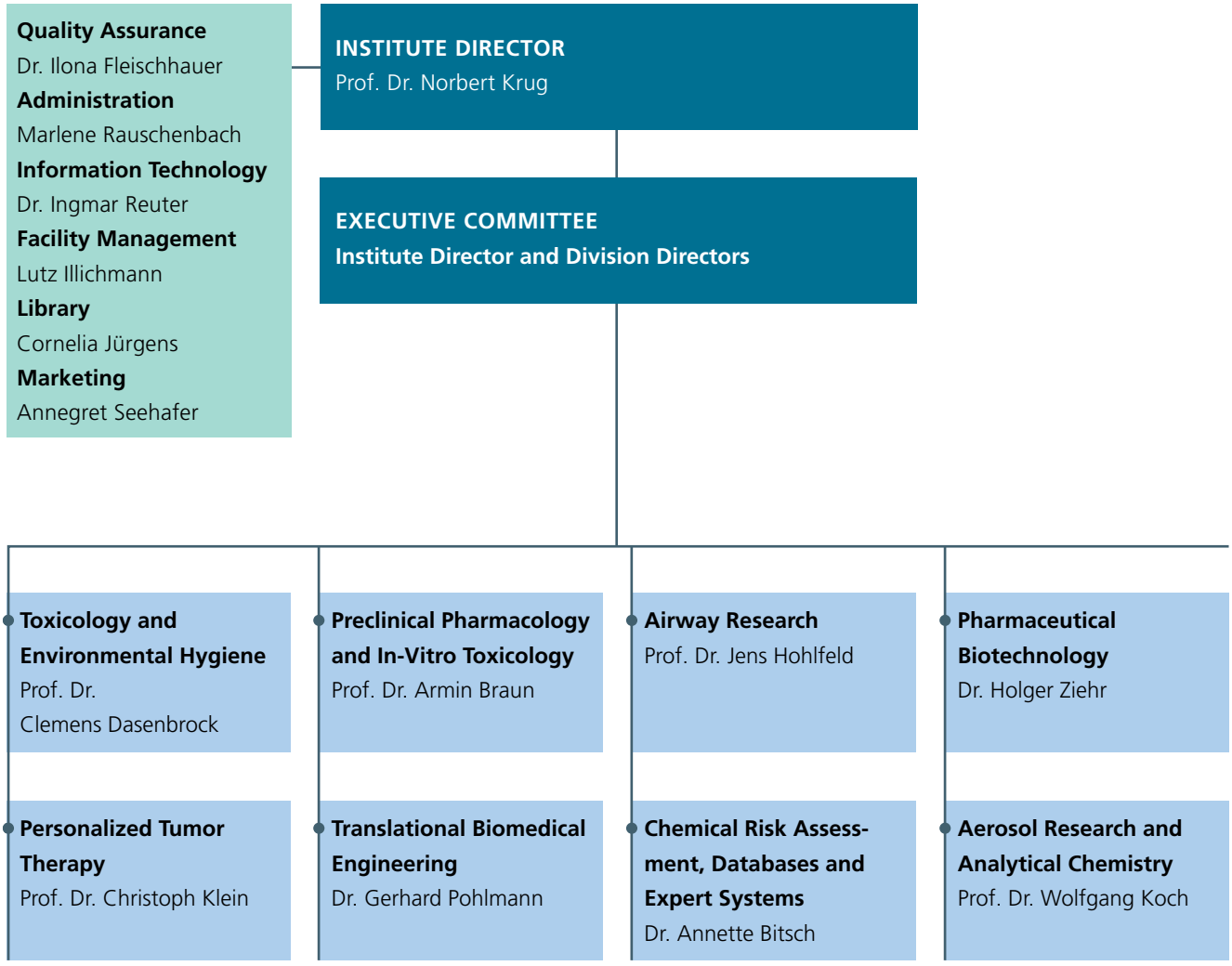
Bringing medical devices from the laboratory into clinical trials

Medical devices make a significant contribution towards improving patients' quality of life. Numerous universities and research laboratories are continuously developing new and innovative solutions to further improve patient care. In the field of translational biomedical engineering, we aim to bring medical devices from the lab into phase I of clinical development, a process that has become rather challenging with the new EU-wide Medical Device Regulation, in particular for small and medium-sized enterprises and research institutions. In spring 2017, the High-Performance Center Translational Biomedical Engineering was inaugurated. Collaborators in this new High-Performance Center in Hannover include Fraunhofer ITEM, the Hannover Medical School, Laser Zentrum Hannover, Leibniz University of Hannover, and in particular the two clusters of excellence REBIRTH and Hearing4all (in Hannover), besides research consortia such as "Biofabrication for NIFE". The Center is funded by the Lower Saxony government and the Fraunhofer-Gesellschaft. The focus at present is on inhalers as smart drug devices and on implants such as cochlear implants.

Personalized tumor therapy

The focus of the Fraunhofer ITEM Division of Personalized Tumor Therapy is on the development of diagnostic tests and innovative models to enable detection of disseminated cancer cells early in the disease and prediction of the response to therapy of metastatic progenitor cells. The division closely collaborates with the Chair of Experimental Medicine and Therapy Research of the University of Regensburg.

ORGANIZATIONAL STRUCTURE



as at January 2018

Prof. Norbert Krug has been Executive Director of Fraunhofer ITEM since January 1, 2017.

Headed by the Institute Director and the Executive Committee, Fraunhofer ITEM is organized in eight divisions, which have pooled their expertise in three business units: Drug Development, Chemical Safety and Assessment, and Translational Biomedical Engineering. The two youngest divisions – "Translational Biomedical Engineering" and "Personalized Tumor Therapy" – were instituted at the beginning of 2017.

The Fraunhofer ITEM headquarters are in Hannover, the institute's Division of Pharmaceutical Biotechnology has its facilities in Braunschweig on the campus of the Helmholtz Center for Infection Research, and the Division of Personalized Tumor Therapy is based in Regensburg's BioPark.

GXP – QUALITY ASSURANCE ACCORDING TO INTERNATIONAL STANDARDS

Fraunhofer ITEM is striving to meet high quality standards with the services and products offered and to ensure maximum safety for trial subjects in clinical studies performed at the institute. Not only are the relevant legal regulations strictly complied with, but state-of-the-art regulatory requirements are invariably taken into consideration. To guarantee that the work performed at Fraunhofer ITEM satisfies internationally accepted quality standards, Fraunhofer ITEM has implemented the GXP quality assurance systems. These include Good Laboratory Practice (GLP), Good Clinical Practice (GCP), and Good Manufacturing Practice (GMP). With their respective scopes of application, these quality assurance systems cover the translational approach in the institute's spectrum of activities. The central service unit "Quality Assurance" is responsible for putting into practice the relevant quality assurance programs.

GLP compliance of non-clinical safety studies

To ensure reliability and traceability of the data generated in non-clinical health and environmental safety studies, the GLP principles include, among others, the following requirements:
– Clear assignment of responsibilities within the test facility
– Meticulous planning and qualified performance of every study
– Complete documentation of all procedures and preparation of comprehensive reports

By means of study-based and facility-based inspections, the service unit "Quality Assurance" continuously monitors compliance with these principles in the institute's departments that are concerned with toxicology, safety pharmacology, and analytics. For more than two decades, the competent authorities have performed regular inspections and have certified the institute's GLP compliance for a broad range of studies. The most recent inspection in December 2017 was also successful. The established quality assurance system thus guarantees to all sponsors an internationally recognized quality standard in the institute's non-clinical departments.

GCP standard of clinical trials

The ethical principles for biomedical research laid down in the Declaration of Helsinki form the basis of the GCP principles describing the quality standards to be met in clinical trials. At Fraunhofer ITEM, long-established quality assurance measures ensure that these requirements are met in trials falling under the German Drug Act and performed on behalf of international sponsors and also in clinical research projects. The service unit "Quality Assurance" assists the clinical investigators in fulfilling their responsibilities by closely monitoring implementation of the quality-relevant processes under aspects of GCP and by routinely checking the corresponding documentation. The institute's sponsors have rated the quality level reached as GCP-compliant.

In the Clinical Research Center Hannover (CRC Hannover), co-operated as a Fraunhofer research institution by Fraunhofer ITEM, the Hannover Medical School (MHH) and the Helmholtz Center for Infection Research (HZI), the service unit "Quality Assurance" performs cross-project and coordinating tasks in

the field of quality assurance, thereby maintaining a high level of uniform quality standards in the CRC Hannover facilities. The synergies resulting from the scientific cooperation of the partners in the CRC Hannover thus go hand in hand with guaranteed maximum protection of all trial subjects and fulfillment of sponsors' quality requirements.

GMP quality standard

The Division of Pharmaceutical Biotechnology in Braunschweig has comprehensive expertise and a long track record in the development of GMP manufacturing processes for biopharmaceuticals. For this purpose, the division has established a GMP quality assurance system to ensure compliance with the German Drug Act, the German Ordinance on the Manufacturing of Medicinal Products and Active Ingredients (AMWHV), and the European Union GMP Guide. Other guidelines are also taken into account, e.g. those of the ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use).

The division is operating clean rooms of grades D to B according to Annex 1 of the EU GMP Guide, subdivided into different zones satisfying the respective hygiene and pressure requirements, and using steam and water in the qualities prescribed by the European Pharmacopoeia. All critical equipment for the manufacture of medicinal products has been qualified in compliance with Annex 15 of the EU GMP Guide. An automated filling machine enclosed in a restricted-access barrier system (RABS) of clean-room grade A is available for manufacturing of small batches of sterile investigational medicinal products (IMPs) for use, for example, in clinical trials or stability tests.

The division has been repeatedly inspected by the authorities – the most recent inspection was successfully completed in September 2017 – and holds a manufacturing and importation license for biopharmaceutical APIs based on microorganisms and animal cells and for IMPs.

Biopharmaceutical products can thus be developed in collaboration with industrial and academic partners and can consistently be manufactured to the required quality – from initial cell line development via the optimization of production steps to the released IMP.

CONTACT
Dr. Ilona Fleischhauer
Head of Quality Assurance at the
Hannover site
Phone +49 511 5350-304
ilona.fleischhauer@item.fraunhofer.de

Dr. Neophytos Papamichael
Head of Quality Assurance at the
Braunschweig site
Phone +49 531 6181-6200
neophytos.papamichael@item.fraunhofer.de

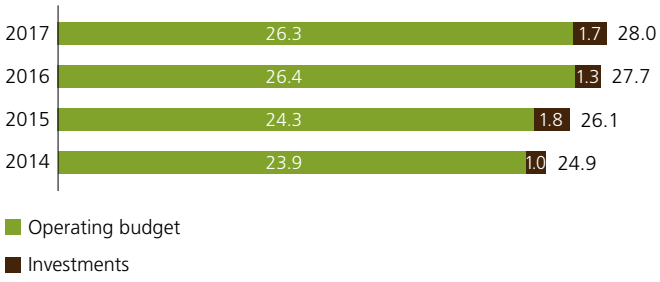
STAFF AND INSTITUTE BUDGET PERFORMANCE

At the end of 2017, Fraunhofer ITEM staff amounted to 320 persons:
9 apprentices
41 students (including Ph.D. students)
270 scientific, technical, and administrative staff

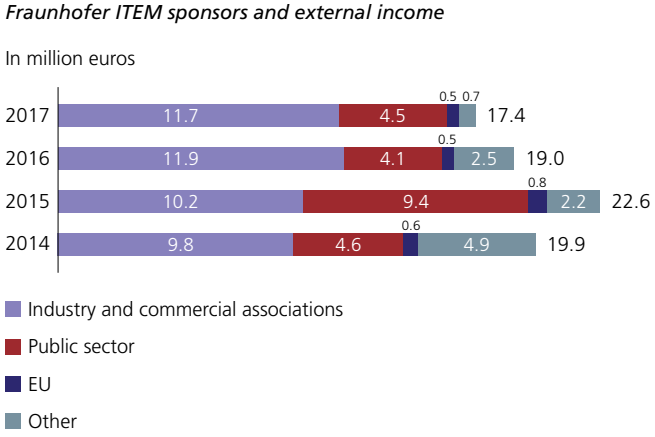
In 2017, the institute's budget reached a level of 26 million euros. Financing by acquired funding amounted to 64 percent. The share of industrial income in the institute's budget was 45 percent. Investments of Fraunhofer ITEM amounted to approximately 1.7 million euros.

Fraunhofer ITEM staff

Fraunhofer ITEM total budget



Fraunhofer ITEM sponsors and external income



BOARD OF TRUSTEES

The boards of trustees of the individual Fraunhofer Institutes act as purely advisory bodies to their institute's management. The members come from academia, industry, and government agencies. In 2017, the Fraunhofer ITEM board or trustees was made up of the following members:

Dr. Eckhard von Keutz
Chairman of the board of trustees
Head of Early Development,
Drug Discovery, Pharmaceuticals, Early Development,
Bayer AG

Prof. Dr. Christopher Baum
Deputy Chairman of the board of trustees
President and member of the Presidential Council
responsible for the Division of Research and Teaching of the
Hannover Medical School

Dr. Marcus Beiner
Deputy Head of the Department Research and Innovation,
Head of the Division of Life Sciences, Humanities,
Social Sciences, and Sustainable Development,
Lower Saxony Ministry of Science and Culture

Prof. Dr. Dieter Bitter-Suermann
Former President and member of the Presidential Council
responsible for the Division of Research and Teaching of the
Hannover Medical School

Prof. Dr. Ulrich Deschl
Head of Nonclinical Drug Safety,
Boehringer Ingelheim Pharma GmbH & Co. KG

Prof. Dr. Hillel S. Koren
Managing Director, Environmental Health, LLC;
former Director Human Studies Division,
United States Environmental Protection Agency;
Research Professor Carolina Environmental Program,
University of Carolina at Chapel Hill, USA

Dr. Edgar Leibold
Vice President Product Stewardship,
BASF SE

Prof. Prof. h. c. Dr. med. Thomas Lenarz
Professor and Chairman of the Department of
Otorhinolaryngology and Director of Deutsches HörZentrum,
Hannover Medical School

Prof. Dr. Reinhard Pabst
Lower Saxony Professorship in Immunomorphology,
Hannover Medical School

Prof. Dr. Klaus F. Rabe
Medical Director and Executive Medical Officer,
LungenClinic Grosshansdorf;
Endowed Professorship in Internal Medicine/Pneumology,
Faculty of Medicine, Kiel University

Prof. Dr. Gerhard Schlüter
Consultant in toxicology;
former Global Head Toxicology, Bayer HealthCare AG

Dr. Thor A. Voigt
Medical Director Germany,
Boehringer Ingelheim Pharma GmbH & Co. KG

Dr. Torsten Wagner
Senior Vice President, Corporate Technical Operations,
Merz Pharma GmbH & Co. KGaA

CRC HANNOVER

State-of-the-art center for clinical research

The Clinical Research Center Hannover (CRC Hannover) is a center for early-phase clinical trials that is the only one of its kind in Germany, used collaboratively by three well-established research institutions: Hannover Medical School (MHH), Helmholtz Center for Infection Research (HZI), and Fraunhofer ITEM. As a proof-of-concept center it provides a platform for safety and efficacy testing of novel drugs, diagnostic methods and medical devices on their way to marketing authorization. In addition to proof-of-concept trials, HZI is conducting the "German National Cohort" study, the largest health study in Germany, at the CRC Hannover. Over the next few years, 10,000 individuals will be examined and questioned here. The aim of the study is to provide information facilitating early detection, prevention, and treatment of wide-spread conditions such as cardiovascular and respiratory diseases, cancer, diabetes, dementia, infections, and diseases of the immune system.

For the performance of phase-I studies (first-in-man trials with novel drugs to test their safety in a small number of volunteers) and phase-II studies (required to provide the proof of concept of novel medications or therapeutic approaches in man), a total of 50 beds are available, 30 of which allow intensive monitoring of study participants. The technical equipment in the CRC Hannover enables comprehensive diagnostics, complemented by the additional infrastructure of the three cooperating research institutions. Studies at the CRC Hannover, however, are not limited to early-phase clinical trials. In a recent phase-IV study, for example, Fraunhofer ITEM investigators demonstrated a bronchodilator combination drug that had already been approved for COPD treatment to have a positive effect on the heart function of COPD patients as well.

The first-rate equipment available at the CRC Hannover allows the Fraunhofer scientists to do airway research at a high level. For example, they have at their disposal a cutting-edge MRI scanner with a xenon polarizer. This imaging technology allows them to visualize not only lung tissue, but also the air in the lungs and even the air passing into tissue. The establishment of this method represents a milestone, in particular for the search for biomarkers that are suitable to indicate whether lung tissue is healthy or diseased. Such diagnostic biomarkers in turn can then be used to develop new methods for drug testing.

The CRC Hannover furthermore hosts one of the most modern biobanks in Germany: the Hannover Unified Biobank (HUB) of the Hannover Medical School – a highly automated, state-of-the-art depository for biomaterials with affiliated preanalytics. This is a great benefit to the institutions cooperating in the CRC Hannover: it gives them the possibility to store biomaterials from patients required for medical research – under high quality standards. The HUB is one of only few biobanks in Germany that have been certified in accordance with DIN EN ISO 9001:2008.

Besides offering state-of-the-art facilities for medical research, the CRC Hannover is also in high demand as a conference center. For example, the CRC Hannover each year hosts the Fraunhofer seminar "Models of Lung Disease", organized by Fraunhofer ITEM in close cooperation with the German Center for Lung Research (DZL). This two-day event provides an international platform for intense discussions between industry, academia and authorities about predictive disease models and translational lung research, accompanied by scientific poster presentations. Another example of the CRC Hannover being used as a convention center is the "Pulmonary Fibrosis" patient seminar, organized at regular intervals by BREATH, the Hannover DZL site. The TRAIN Academy professional education program "Translational Research & Medicine: From Idea to Product" is yet another series of lectures the CRC Hannover hosts at regular intervals, besides numerous other external and internal events.

CONTACT
Prof. Dr. med. Norbert Krug
Phone +49 511 5350-8100
norbert.krug@item.fraunhofer.de

CRC HANNOVER

SELECTED NEWS

German-Australian iCAIR project launched by Fraunhofer

In the Fraunhofer International Consortium for Anti-Infective Research – iCAIR in brief – researchers from Fraunhofer ITEM have teamed up with colleagues from the Hannover Medical School and Griffith University's Institute for Glycomics in Australia. They have set themselves the ambitious goal of developing new anti-infective drugs. (The photo shows the project managers from the collaborating institutions (from left to right): Prof. Armin Braun, Fraunhofer ITEM, Prof. Rita Gerardy-Schahn, Hannover Medical School, and Prof. Mark von Itzstein, Griffith University.) At Fraunhofer ITEM, this pioneering collaboration was officially launched on January 18, 2018. Embedded in the seminar "Models of Lung Disease" 2018, representatives from academia, industry, governmental institutions and from the Australian embassy got together to celebrate this launch.

CRACK IT Challenge 2017 – great success for Fraunhofer ITEM

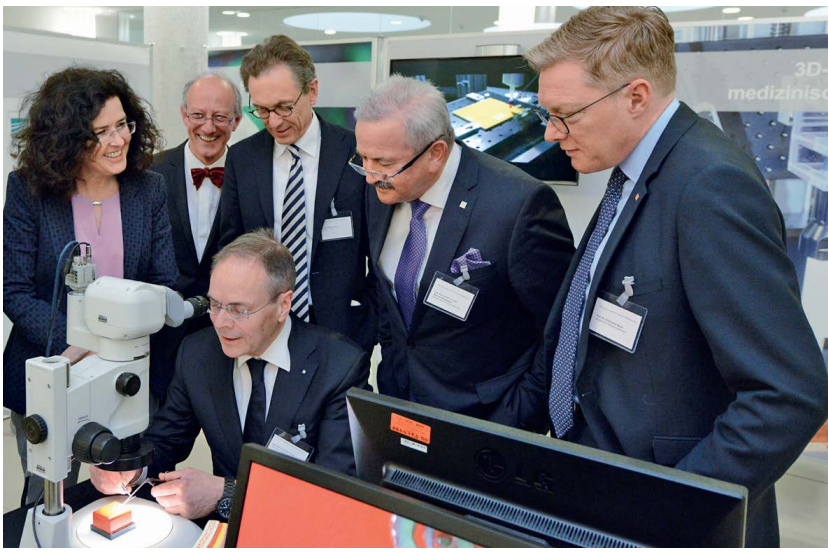
Two Fraunhofer ITEM teams have been awarded funding for their research projects in the 2017 CRACK IT Challenge competition, which brings together large industries, academia and SMEs to develop marketable products or improve business processes that will have a significant impact on the use of animals in research. The CRACK IT Challenge is the NC3Rs' response to the changing environment in the biosciences. The NC3Rs is a UK-based scientific organization dedicated to replacing, refining and reducing the use of animals in research and testing.

Establishing bacteriophages as an approved drug

Bacteria worldwide keep developing new resistances to antibiotics. Alternative therapies are urgently needed to meet this challenge. In the collaborative project Phage4Cure, Fraunhofer ITEM, Leibniz Institute DSMZ, Charité Berlin, and Charité Research Organisation GmbH have taken on this challenge. Their goal is to establish bacteriophages as an approved drug for treating bacterial infections. The German Federal Ministry of Education and Research is funding this project with almost four million euros over a period of three years.

New High-Performance Center to optimize translation in biomedical engineering

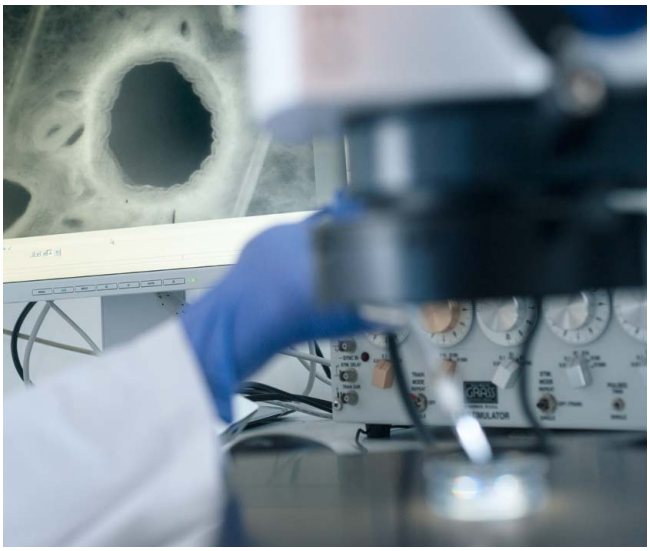
In spring 2017, Dr. Gabriele Heinen-Kljajić (far left on the photo), Lower Saxony Minister of Science and Culture, and Prof. Reimund Neugebauer (second from the right), President of the Fraunhofer-Gesellschaft, inaugurated the High-Performance Center Translational Biomedical Engineering together with representatives from industry, government and academia (Prof. Theodor Doll (second from the left), Head of the High-Performance Center, Prof. Norbert Krug (third from the left), Fraunhofer ITEM Director, Prof. Christopher Baum (far right), President of the Hannover Medical School, and Prof. Thomas Lenarz (sitting at the front), Chairman of the Department of Otorhinolaryngology of the Hannover Medical School). The High-Performance Center is aimed at bringing medical devices from the lab into phase I of clinical development and at helping to overcome scientific and economic hurdles of the development process, in particular with regard to the new EU-wide Medical Device Regulation. Collaborators in this new High-Performance Center in Hannover

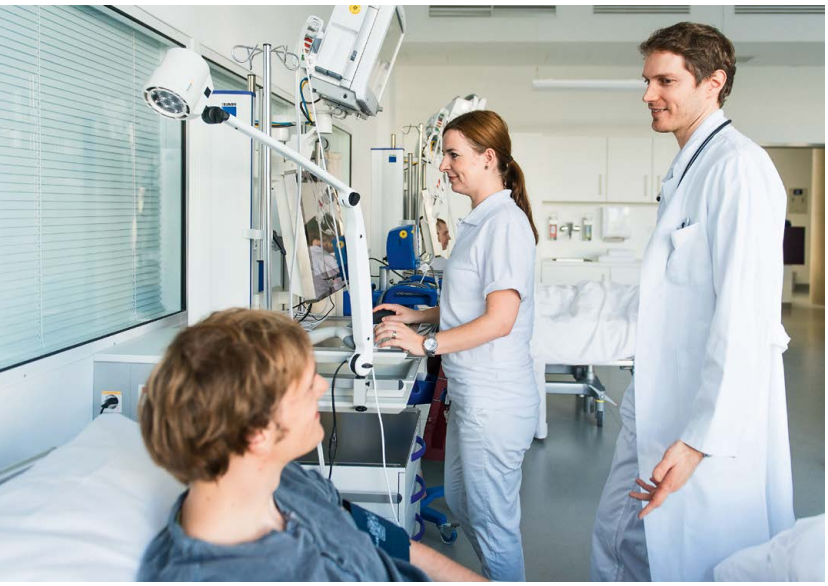


include Fraunhofer ITEM, the Hannover Medical School, Laser Zentrum Hannover, Leibniz Universität Hannover, and in particular the two clusters of excellence REBIRTH and "Hearing4all" (in Hannover), besides research consortia such as "Biofabrication for NIFE". The Center is funded by the Lower Saxony government and the Fraunhofer-Gesellschaft.

Development of novel in-vitro test systems using bioprinting

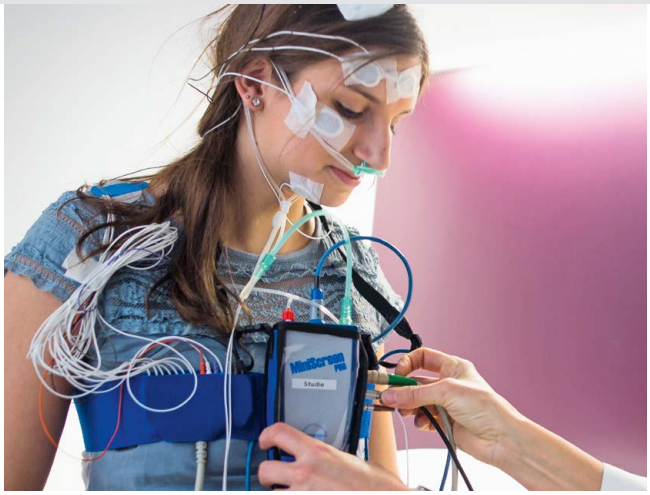
Valid preclinical testing of new therapeutic drugs requires predictive and available test systems. Three strong partners have joined forces in a research collaboration aimed at developing novel in-vitro test systems with muscle cells from different tissue regions: Aspect Biosystems Ltd. (Vancouver, Canada), InSCREENeX GmbH (Braunschweig, Germany), and Fraunhofer ITEM. The aim is to use functionally immortalized muscle cell lines to produce human 3D tissue models of consistent quality by means of bioprinting and validate their functionality. Fraunhofer ITEM scientists are validating the 3D tissue models based on viable human tissue slices (photo: analysis of bronchoconstriction in a precision-cut lung slice).





Start of proof-of-concept initiative

The proof-of-concept initiative is a pilot project initiated by the Helmholtz Association, Deutsche Hochschulmedizin (peak organization of German university hospitals and medical schools) and the Fraunhofer-Gesellschaft to promote cross-organizational collaboration in translational health research. The initiative is intended to lead promising development projects to successful proof of concept in patients. To this end, the collaborating organizations want to pool available competencies and infrastructure for the development of innovative methods of disease diagnosis, prevention, and therapy in a common platform open to all scientific institutions. The Helmholtz Association and the Fraunhofer-Gesellschaft each have allocated six million euros for this pilot project. This will enable funding of four to six innovative development projects that will be selected in a competitive application process. Fraunhofer ITEM is involved in 19 out of 80 project proposals submitted under the proof-of-concept initiative. It is expected that this pilot phase will evolve into a sustainable element of the funding environment, allowing the initiated projects to be continued.



New sleep laboratory set up at the CRC Hannover

Fraunhofer ITEM has extended the diagnostic possibilities in its clinical research by setting up a sleep laboratory in the phase-I unit of the CRC Hannover. The aim of a first study performed in collaboration with the Hannover Medical School is to investigate the effects of a new drug on the symptoms of depressive patients, but also on sleep disorders and other psychosomatic problems such as anxiety. Fraunhofer ITEM in Hannover is one of five study centers in Germany participating in this study.

Paradigm shift in toxicological testing

To promote the required paradigm shift in toxicological testing is the aim of the flagship project EU-ToxRisk, with the ultimate goal of delivering testing strategies that will enable reliable, animal-free hazard and risk assessment of chemicals. Scientists from Fraunhofer ITEM are contributing to this project in many ways. For example, they are leading three case studies in which groups of compounds are tested by new approach methodologies. In addition, they have devised experimental work to integrate a battery of suitable in-vitro and ex-vivo models into integrated approaches to testing and assessment, IATA in brief.

CARDIOR

Cooperation initiated with Cardior Pharmaceuticals GmbH

Cardior Pharmaceuticals GmbH, a spin-off company from the Hannover Medical School headed by Prof. Dr. Dr. Thomas Thum, develops RNA-based therapeutics for the treatment and prevention of heart disease. Fraunhofer ITEM accompanied Cardior in setting up a product development program, has performed scientific preclinical pharmacology and toxicology studies on Cardior's first drug candidate and, in addition, is supporting the company with its regulatory expertise.

Non-animal testing of novel antibiotics

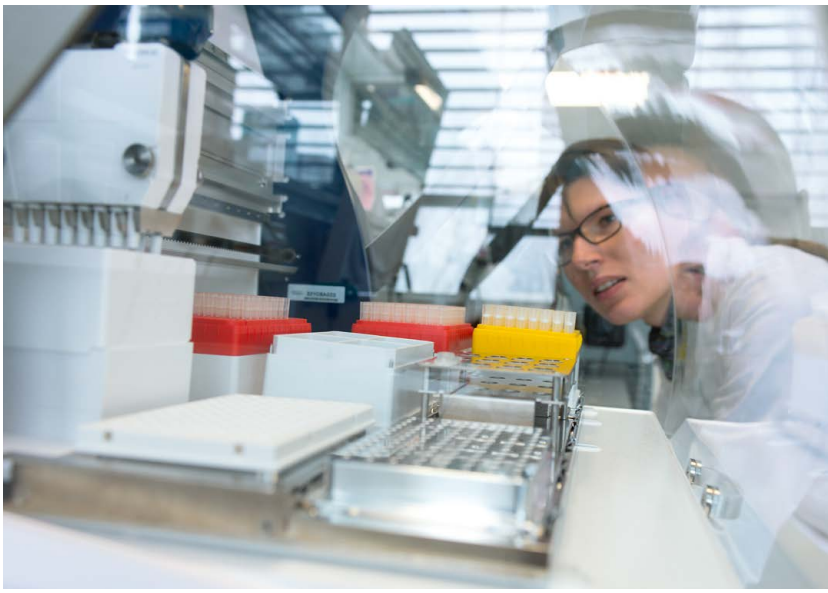
The options currently available for non-animal testing of novel antibiotics are strongly limited. This is why the German Federal Ministry of Education and Research is funding the project Inhal-Ab, aimed at establishing a test battery of in-vitro and ex-vivo models of the lung for preclinical testing of inhalable antibiotics as alternatives to animal testing. These alternative models are planned to replace animal experiments in the dose-finding studies required by current legislation and to help provide the proof of concept for novel inhalable antibiotics and formulation additives aimed at optimizing drug targeting. For non-animal testing of antibiotics, Fraunhofer ITEM is evaluating a combination of alternative models using human cell lines, the "isolated perfused rat lung" (IPL), and precision-cut lung slices (PCLS) from rats as well as human tissue.

Gerhard Domagk Prize for Cancer Research

Prof. Christoph Klein, Fraunhofer ITEM Division Director of Personalized Tumor Therapy and Head of the Department of Experimental Medicine and Therapy Research of the University of Regensburg, was awarded the Gerhard Domagk Prize for his pivotal findings on mechanisms of early metastatic spread in breast cancer, which were published in the renowned journal "Nature". With these findings the researcher threw into doubt the long established oncological dogma that cancer cells seed above all from advanced tumors. The Gerhard Domagk Prize is awarded by the eponymous foundation in cooperation with the University Society of the University of Münster (Germany) to honor internationally outstanding results of cancer research that have received much attention.

New Working Group on High-Throughput Drug and Target Discovery

The low success rate in the generation of predictive, disease-relevant cell models is among the major obstacles to the discovery and development of novel therapies for most cancer types. To help solve this problem, a new Working Group on High-Throughput Drug and Target Discovery was set up at Fraunhofer ITEM in Regensburg in September 2017. This new working group first wants to generate patient-derived preclinical in-vitro and in-vivo models for a broad spectrum of cancer types. These will then be used for genetic and pharmacological high-throughput screenings to identify disease-relevant genes, signaling pathways, therapies, and diagnostic applications.



eTRANSAFE – for more safety in the drug development process

The 40 million euro European project "Enhancing Translational Safety Assessment through Integrative Knowledge Management" – eTRANSAFE – was launched in September 2017, aimed at speeding up the development of better and safer medicines for patients. The project consortium is a private and public partnership of eight academic institutions, six SMEs, and twelve pharmaceutical companies. One of the project partners is Fraunhofer ITEM. The aim is to develop an advanced data integration infrastructure together with innovative computational methods to improve safety assessment across the drug discovery and development process. The assignment of Fraunhofer ITEM toxicologists and physicians in this project is to evaluate whether and to what extent preclinical data can be used to predict clinical findings.

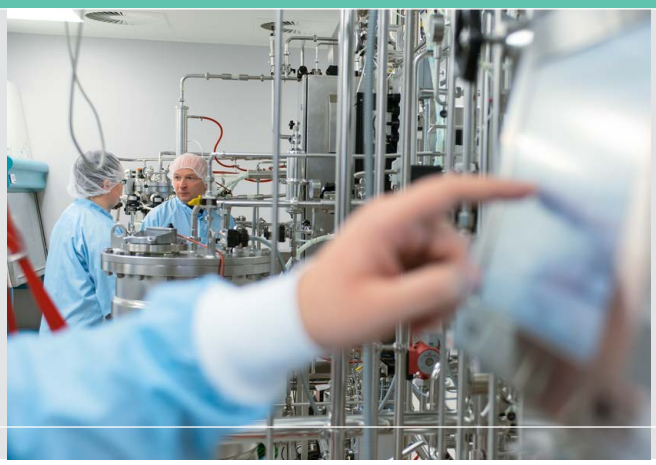
DRUG DEVELOPMENT

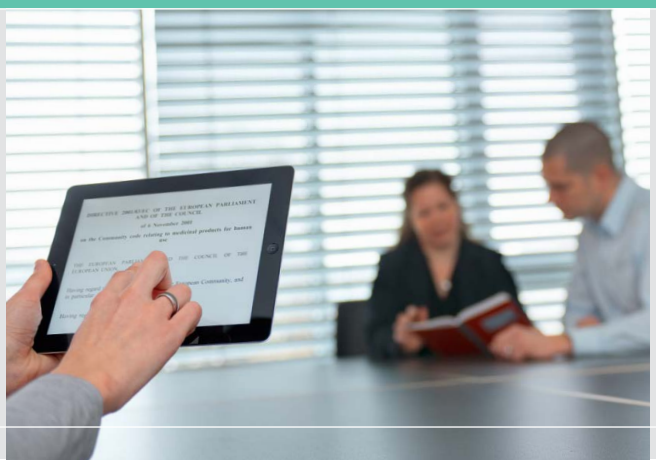
OUR SERVICES: FROM DRUG CANDIDATE TO PROOF OF CONCEPT

We are committed to translating innovative drug research into therapeutic applications – safely, reliably and efficiently. Based on our scientific expertise, we offer appropriate methods and approaches to this end. With custom-tailored development strategies, we support our clients in process development for and manufacturing of active biopharmaceutical ingredients and sterile investigational medicinal products, in preclinical testing – both pharmacology and toxicology – and in early-phase clinical trials from first-in-human to the clinical proof of concept.

Our state-of-the-art equipment and innovative research approaches allow us to develop new methods and techniques – also in cooperation with our clients. Already in the early phase of drug development, we provide assistance as independent consultants and negotiators in the dialog between applicant and regulatory authority. We work in compliance with regulatory and legal requirements for drug development and according to the quality assurance systems GLP, GMP, and GCP.

With the services offered by Fraunhofer ITEM, we can cover either the complete drug development chain or individual phases on the way from the drug candidate to clinical trials.





Development of novel biopharmaceuticals

A multidisciplinary team of biologists, chemists, pharmacists, engineers, and technicians assists our clients on their way from the idea for a new biotherapeutic via development of a production cell line to GMP manufacturing of the investigational medicinal product (IMP) released for use in clinical trials. This team guides you along the entire regulatory pathway to your approved IMP dossier. Our clients benefit from our profound knowledge accumulated over 25 years from a broad range of biopharmaceutical candidates – from simple proteins to complex structures such as viruses and cells. Our service portfolio includes:

- Technical and regulatory consultancy for biopharmaceutical development projects, in particular on recombinant proteins and antibodies
- Engineering of recombinant mammalian and microbial production cell lines
- GMP manufacturing, cell banking and storage of master and working cell banks
- Development of complex upstream and downstream sequences with subsequent upscaling
- GMP manufacturing of API pilot charges
- Release testing of biopharmaceutical APIs and IMPs
- Aseptic filling and quality-assured release of IMPs (liquid dosage forms)

Regulatory research and risk assessment in drug development

Fraunhofer ITEM has combined its expertise in drug research and development with its experience in registration and risk assessment of chemicals. With these forces joined, the institute is uniquely positioned to support clients in regulatory affairs in the drug development process. Our scientists explore, develop, and validate new approaches to manufacture, characterize, and test innovative medicinal products. Furthermore, we ensure regulatory input on these approaches and implement them in product development in cooperation with the client. Our service portfolio includes:

- Preparation of a regulatory strategy to take products from lab to market
- Interaction with regulatory authorities
- Preparation of the required documentation
- Risk assessment
- Regulatory research

Preclinical testing

For preclinical development of a drug candidate we offer a broad spectrum of disease-relevant and toxicological models. Our outstanding expertise, many years of experience with partners from the pharmaceutical and biotech industries, and state-of-the-art equipment provide the foundation for our scientific solutions and custom-tailored services. Our special focus is on inhalation toxicology and immunotoxicology.

For efficacy testing of drug candidates we offer disease-relevant models for all therapeutically relevant diseases of the respiratory tract such as COPD, asthma, pulmonary fibrosis, infections, and tumors. We are committed to enabling reliable prediction of the efficacy of drug candidates – by constant development of new methods in collaboration with academic institutions and research centers. For toxicology testing of drug candidates we offer the following services and expertise:

- In-vitro studies (genotoxicity, molecular toxicity, screening assays)
- Ex-vivo studies (e.g. precision-cut lung slices)
- In-vivo studies (relevant species, single-dose and repeated-dose toxicity)
- Safety pharmacology (core battery)
- Testing strategies to accompany clients during scientific advice and registration processes
- Track record including biopharmaceuticals, oligonucleotide-based therapeutics, and ATMPs
- Study performance according to OECD GLP, where applicable

Clinical trials

Finding the most appropriate model for your proof of concept and the most suitable study design are challenges we can successfully handle with our excellent medical expertise and strong academic background. We support clients in the development of drugs targeting respiratory and allergic diseases and do patient-oriented research to help people suffering from these conditions. A broad range of challenge models is available for clinical studies on respiratory diseases such as asthma, allergic rhinitis, COPD, and interstitial lung diseases (idiopathic pulmonary fibrosis in particular). In addition, a new sleep laboratory will extend our study portfolio as from 2018. In the state-of-the-art CRC Hannover, we perform our studies with a highly qualified and dedicated team of physicians, study nurses, and medical documentation specialists, accompanied by an independent quality assurance unit. The following services and infrastructure are available:

- Fraunhofer Challenge Chambers: challenge chambers for proof-of-concept studies with sophisticated study designs, enabling exposure of test subjects to natural pollen, allergen extracts, ozone, or hypoxia challenge.
- Inhaled allergen challenge
- Segmental challenge during bronchoscopy
- Exercise testing (spiroergometry)
- Collection and analysis of human samples with subsequent storage in the biobank at the CRC Hannover
- Biomarker analysis
- Imaging: non-invasive MRI techniques
- In-house GMP laboratory for production of intravenous dosage forms of IMPs
- Patient/volunteer database

PROJECTS

Fraunhofer ITEM strengthens infection research

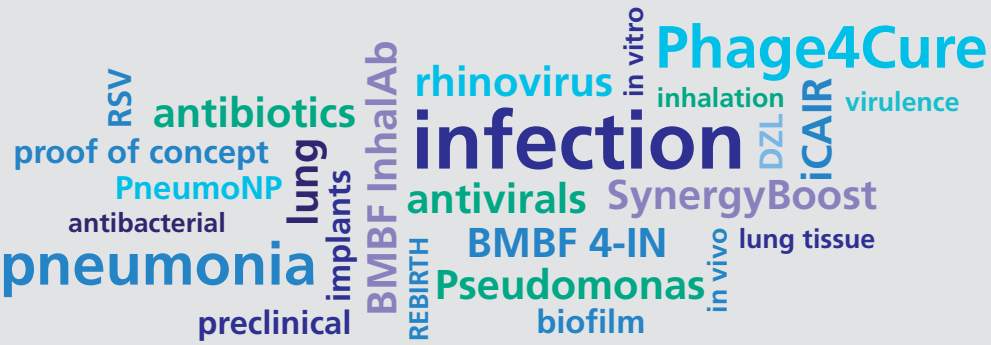
Infectious diseases pose an increasing global threat, due to their rapid spread and the ever faster development of resistances to antibiotics. Novel therapies, therefore, are urgently needed, but these also require new cross-disciplinary approaches in research. Building on its extensive experience in the fields of respiratory diseases, testing of new drug candidates, and their translation from bench to bedside, Fraunhofer ITEM is extending its research on infections and their treatment. For efficacy testing, custom-tailored infection models are being developed, using, for example, antibiotic-resistant biofilms, human tissue, and inhaled administration. The institute is contributing this knowledge as a partner in publicly funded projects, such as InhalAb and 4-IN, two projects funded by the German Federal Ministry of Education and Research for the development of alternative test methods for inhaled antibiotics, and to their use for testing novel insect-based drugs. Viral lung infections are being studied in collaboration with the pharmaceutical industry and within the German Center for Lung Research. Furthermore, Fraunhofer ITEM and the Hannover Medical School together have initiated a strategic alliance with Griffith University, Australia, aimed at setting up a proof-of-concept center for the development of anti-infective therapies in the collaborative project iCAIR. By extending its activities in infection research, Fraunhofer ITEM wants to make a contribution in the fight against the threat from infections.

CONTACT
Dr. Sabine Wronski
Phone +49 511 5350-444
sabine.wronski@item.fraunhofer.de

Bacteriophages as an alternative therapeutic for treating bacterial infections

Bacteria worldwide keep developing new resistances to antibiotics. Alternative therapies for treating bacterial infections are thus urgently needed. A promising therapeutic option are lytic bacteriophages – viruses that highly specifically recognize, lyze, and kill bacteria of a particular strain without harming a patient's natural flora or attacking his or her own cells. In former USSR countries in particular, they have been successfully used for decades to treat bacterial infections. Due to insufficient and non-standardized bacteriophage production and missing clinical trials, however, they have never received regulatory approval as drugs. In the project Phage4Cure, Fraunhofer ITEM, Leibniz Institute DSMZ, Charité Berlin, and Charité Research Organisation have teamed up to develop and establish a manufacturing process for phages for therapeutic use in compliance with defined quality standards. The scientists are planning to test an exemplary phage-based product in preclinical studies in tissue and animal models. Thereafter, a clinical trial will be performed to demonstrate the safety and tolerability of the inhaled medicinal product. In the next stage, the drug product shall be advanced towards authorization for the first time ever and a new model authorization process for phage-based products shall be worked out. Fraunhofer ITEM's contribution to this project is focused on the manufacturing process and toxicological studies. The project is coordinated by Fraunhofer ITEM and funded by the German Federal Ministry of Education and Research.

CONTACT
Dr. Anton Roß
Phone +49 531 6181-6300
anton.ross@item.fraunhofer.de



Infectious diseases are the leading cause of death worldwide. Fraunhofer ITEM scientists are breaking new ground in research on infections.

In-vitro testing of therapeutic nanosystems against bacterial lung infections

Infections caused by antibiotic-resistant bacteria today are among the greatest healthcare challenges worldwide. The main reason for this is the lack of effective antibiotic treatment options. To address this problem, scientists are developing new approaches, among them novel nanocompounds as carriers for combined antibiotic systems. Administration of such antibiotic nanosystems to the lung in the form of aerosols is the first choice for treating airway infections. In the EU project PneumoNP, Fraunhofer ITEM scientists are using an in-vitro model with human lung cells for cytotoxicity testing of selected drug candidates coupled to nanosystems. The tests are performed under close to real-life conditions, applying the antibiotic nanosystems in the form of aerosols. To mimic the in-vivo situation, the cells of a lung epithelial cell line are exposed to the nanosystems under investigation at the air-liquid interface by using the Fraunhofer-patented P.R.I.T.® technology. After the treatment, cell viability is compared with that of cells treated with a control aerosol. Using this method, several nanosystems coupled with antibiotic agents were tested for potential cytotoxic effects. The results have shown the combination of the antibiotic agent with the nanosystem carrier to have a major impact on the cytotoxic potency of the drug candidate. The method thus allows potentially toxic candidates to be identified and discarded already at an early stage of drug development.

CONTACT
Dr. Jan Knebel
Phone +49 511 5350-273
jan.knebel@item.fraunhofer.de

Patient-specific cancer therapies in a human micrometastasis model

Metastastatic disease is among the prevailing causes of death in cancer patients. High cellular heterogeneity, mutations differing from those of the primary tumor, and interactions with the microenvironment of the affected organ create challenges that many test systems are unable to meet. Scientists at Fraunhofer ITEM are using viable human lung slices to study the behavior and growth of cancer cells interacting with their natural tumor microenvironment within micrometastases. The patient-specific cancer cells are provided by Fraunhofer ITEM in Regensburg. Metastasized melanoma cells are collected from lymph nodes, labeled by GFP fluorescence, and then cultured. Due to their labeling, cancer cells differ specifically from all other cells in the lung tissue slices. Interactions between micrometastases and immune cells within the lung structures can thus be observed dynamically and in three dimensions by using immunohistological confocal microscopy. This further allows testing of different cancer therapeutics targeting either the microenvironment, cancer cell growth, or genetic aberrations. For instance, the drug vemurafenib affects only about 50 percent of all melanomas that are due to a driver mutation leading to an increased signaling pathway activity. This could be confirmed in the corresponding model with patient-specific melanoma cells, where a 71-percent cell decrease in mutated melanomas was observed after 48 hours.

CONTACT
Sebastian Konzok
Phone +49 511 5350-299
sebastian.konzok@item.fraunhofer.de

Fraunhofer project to establish manufacturing processes for oncolytic viruses

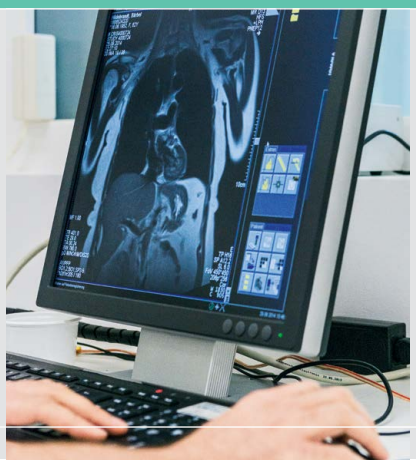
Since April 2017, Fraunhofer ITEM scientists in Braunschweig and Regensburg have been collaborating in an internal Fraunhofer research project. Their ambitious aim is to develop technologies for the development, manufacturing and testing of oncolytic viruses. The task of the researchers in Braunschweig in this project is to develop robust manufacturing processes for these novel therapeutics. Their starting point is a vector based on herpes simplex virus, which shall be developed further to enable targeted infection and killing of cancer cells in non-small-cell lung carcinoma and thus treatment of this type of cancer. The scientists in Braunschweig will first develop cultivation and purification methods, initially based on established methods. They also want to work out a model-based process description that will enable more systematic optimization and prediction of the processes. The new approach comprises iterative improvement of the model, data processing, and data collection, resulting in a steady increase in model reliability as the amount of data grows (keyword: "learning model"). Colleagues from Fraunhofer ITWM (Prof. Karl-Heinz Küfer) will assist the Fraunhofer ITEM scientists. Furthermore, the process development work will be supported by analytical methods. The aim is to thereby also make a contribution to identifying specific requirements for the release of genetically engineered oncolytic viruses.

CONTACT
Dr. Kathrin Bohle
Phone +49 531 6181-6346
kathrin.bohle@item.fraunhofer.de

Safety and toxicity of oligonucleotide-based therapeutics

One focus in the business unit Drug Development is on safety testing of innovative drugs in compliance with regulatory requirements. Four drug candidates of the oligonucleotide class are currently under development. They are DNA or RNA molecules that take their action either through enzymatic processes ("DNAzyme") or by binding complementary nucleic acid sequences. Fraunhofer ITEM was able to successfully contribute its expertise to the non-clinical and clinical testing of HGD40, a DNAzyme for inhaled administration developed by the company sterna biologicals GmbH & Co. KG. Based on this previous experience, a collaborative project with the company Cardior Pharmaceuticals GmbH (Cardior) has recently been launched. Cardior is a spin-off company from the Hannover Medical School, aimed at developing new RNA-based therapeutics for the treatment and prevention of heart disease. Fraunhofer ITEM accompanied Cardior in setting up a product development program during the fund-raising process, which was successfully completed in May 2017 by raising 15 million euros in a series-A round. The development plan has been validated by the competent higher federal authority (German Federal Institute for Drugs and Medical Devices) in a scientific advice meeting supported by the drug regulatory experts of Fraunhofer ITEM. This important step formed the basis for the scientific preclinical pharmacology and toxicology studies on Cardior's first drug candidate that are now being performed by Fraunhofer ITEM.

CONTACT
Dr. Henning Weigt
Phone +49 511 5350-329
henning.weigt@item.fraunhofer.de



Magnetic resonance imaging of the heart was used to investigate whether a bronchodilator drug for COPD treatment has a positive effect on the heart function of COPD patients as well.

Bronchodilator therapy improves heart function in patients with COPD

Constricted bronchi and hyperinflated lungs are among the typical signs of chronic obstructive pulmonary disease (COPD). Long-acting bronchodilator combination therapy (beta-mimetics and anti-muscarinics) represents the most important pillar of treatment in the advanced stage of disease. A placebo-controlled, double-blind clinical trial used magnetic resonance imaging of the heart to investigate whether 14-day treatment with a long-acting combination drug (indacaterol/glycopyrronium, Novartis) would result in improved function not only of the lung, but also of the heart. Over 60 patients with moderate to severe COPD and hyperinflated lungs were examined at Fraunhofer ITEM. Compared with placebo, the treatment was shown to lead to highly significant and clinically relevant improvement of the hyperinflation and bronchial obstruction. Furthermore, left and right atrial filling volumes were found to have substantially increased, resulting in improved cardiac output. The treatment led to a significant improvement of symptoms and quality of life. These results are fundamental for the therapy of COPD, suggesting that the investigated treatment does not only improve lung function, but also leads to a clinically relevant improvement of heart function in COPD patients. The results were presented at the international congress of the European Respiratory Society in Milan (Italy) in September 2017 and were published in the prestigious journal "The Lancet Respiratory Medicine" (Hohlfeld et al., 2018).

CONTACT
Prof. Dr. Jens Hohlfeld
Phone +49 511 5350-8101
jens.hohlfeld@item.fraunhofer.de

Chip cytometry: chip-based cell analysis – a new technology at Fraunhofer ITEM

Chip cytometry is based on the immobilization of cells on special object slides that are referred to as chips. On such chips, cells can be studied with respect to morphology, expression of surface markers, and intracellular function. Consecutive, iterative staining processes allow a comprehensive immunological and functional characterization of cells. This method enables investigations at the single-cell level and, depending on the cell population, the chips can be stored for up to two years. Chip cytometry is thus superior to other methods of analysis such as flow cytometry, offering the possibility to combine direct optical analyses with repeated staining of single cells, but in particular because the cell material can be preserved after the measurements. At Fraunhofer ITEM, chip cytometry is being validated for induced sputum at present. Induced sputum obtained from the lungs of test subjects often exhibits limited cell numbers, so that the use of chip cytometry is holding promise for advances in immunological characterization. Furthermore, sputum includes cells of different sizes with specific fluorescence properties, placing special requirements on the measurement method. First data showed good comparability with the standard methods flow cytometry and microscopic cell differentiation. Chip cytometry, therefore, is planned to be used already for first explorative sputum analyses in a clinical trial.

CONTACT
Dr. Meike Müller
Phone +49 511 5350-8144
meike.mueller@item.fraunhofer.de

CHEMICAL SAFETY AND ASSESSMENT

OUR SERVICES: FROM RISK ANALYSIS TOWARDS SAFE PRODUCTS

Our commitment is to assess the potential risk from chemical substances, including their use in specific products. We use a tiered approach for this, referred to as integrated testing strategy (ITS).

We offer the studies and services required to assess the potential risks from chemicals to human health and the environment and to register these substances for the intended use. Our portfolio includes industrial chemicals, biocides, food additives, and both human and veterinary medicinal products. In close collaboration with our clients, we gather the data required for substance registration to comply with legal requirements, and we take care of regulatory issues.

With self-initiated research projects, we contribute to the development of novel assessment strategies to help improve and refine existing risk assessment methods and ultimately to minimize the need for experimental studies, in particular animal studies. Examples of such projects are elucidation of structure-activity relationships ((Q)SAR), category approaches such as read across, the setting up of databases, and further development of the TTC concept.

The services offered by Fraunhofer ITEM assist you on the way from risk analysis towards safe products.

Development of test methods and analytical procedures

We offer our clients comprehensive consulting and expert opinions in analytical issues that are often beyond the scope of commercially available routine analyses. In close contact with our clients, we develop custom-tailored analytical strategies. In addition, we offer research and development projects in the field of aerosol research, employing methods of physics, process engineering, and physical chemistry. For problem-solving that meets the client's specific requirements, we offer:

Analytical chemistry

- Development of analytical methods and validation in compliance with the relevant guidelines
- Analytical studies (both GLP and non-GLP) required for registration and authorization
- Targeted metabolomics and both target and non-target analysis of inorganic and organic compounds (e.g. aldehydes/ketones, dyes, pharmaceuticals, BTX, PAHs, pesticides, VOCs, SVOCs, metals, and compounds typical of explosives)
- Characterization of complex mixtures in environmental samples and biological matrices
- Structural elucidation of drug substances and natural products and of their metabolites
- Biomonitoring – determination of the bioavailability of pharmaceuticals and food contaminants and, if applicable, their metabolites, (heavy) metals and other chemicals, and test substances from production and development scenarios
- Protein mass spectrometry, structural elucidation of modified proteins, de-novo sequencing

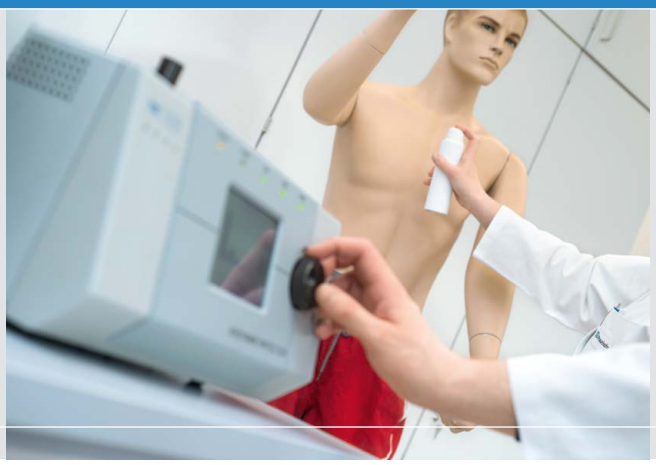
Aerosol research

- Development of instruments and methods for measurement, collection, and generation of aerosols
- Development of methods and technologies for controlled inhalation studies with different atmospheres

Toxicology testing of chemical substances

We offer a broad range of toxicological tests enabling assessment of potential risks from chemicals, particles, complex mixtures, and nanomaterials. Depending on our clients' specific requirements, we develop appropriate testing strategies and, if required, conduct toxicology studies with different routes of administration – with a focus on inhalation toxicology and characterization of inhalable substances. Our service portfolio includes:

- Regulatory assessment by means of standard toxicological tests in compliance with international guidelines (OECD, EU, EPA, or FDA)
- Focus inhalation toxicology:
  - Nose-only and whole-body exposure of rodents
  - Toxicokinetics of inhaled particles
  - Specific lung toxicity measurements incl. bronchoalveolar lavage
  - Inflammatory reactions in the lung
- Focus (nano)particles and fibers:
  - Deposition and retention
  - Particle clearance by using radiolabeled tracers
  - Biopersistence of fibers
  - Bioavailability of metals from solid material particles
- P.R.I.T.® exposure system for in-vitro exposure of cells and tissues to airborne, soluble, and particulate test substances at air/liquid interfaces
- Characterization of molecular mechanisms of action
- Use of our own toxicological databases (RITA, *go*RENI, *Dev*Tox)



Exposure characterization

To characterize occupational, indoor, and environmental human exposure to gases and aerosols/particles, inhalation exposure in particular, we combine state-of-the-art measurement technology with mathematical modeling tools. Whenever necessary, we provide adaptations to customize a solution to a client's specific needs or to guarantee its compliance with relevant regulations. We use the following methods for this purpose:

- Physical and chemical measurement of emissions from aerosols (e.g. dusts, (nano)particles, sprays, oil mists, vapors, and microorganisms) and gases (volatile and semivolatile organic compounds)
- Inhalation exposure modeling:
  - Dispersion of pollutants (SprayExpo, e.g. for biocides; quantification of particle deposition and resuspension for indoor air models)
  - Lung deposition and absorption (interspecies comparison; clearance and solubility)
- Development of custom-tailored measurement and process technology:
  - Measurement technology for dusts and aerosols (PM_{10}, $PM_{2.5}$, exhaust gases, nanoparticles)
  - Aerosol generation methods (calibration aerosols, nebulization, dry dispersion)
- Process development (development of test methods and analytical procedures)
- Design of relevant exposure scenarios and calculation of the exposure – also by using commercially available models
- Development of new exposure models in collaboration with regulatory agencies and/or industrial clients

Regulatory research and risk assessment of chemicals

To assess the potential risk from chemical substances – industrial chemicals, biocides, food additives, and human and veterinary medicinal products – including their use in specific products, we use a tiered approach, referred to as integrated testing strategy (ITS). With self-initiated research projects, we contribute to the development of novel assessment strategies to help improve and refine existing risk assessment methods and ultimately to minimize the need for experimental studies, in particular animal studies. Examples of such projects are elucidation of structure-activity relationships ((Q)SAR), category approaches such as read across, the setting up of databases, and further development of the TTC concept. For risk assessment of chemicals and their registration for a particular use, we offer:

- Data gap analysis and literature search: in cooperation with the sponsor, we determine what data are available and whether additional studies are necessary, and we check whether there is information publicly available about the substance in question.
- Preparation of dossiers: we prepare IUCLID-5 datasets for the studies, perform exposure and risk assessments, and prepare a chemical safety report (CSR) and the registration dossier.
- Consulting and support to develop a registration strategy tailored to your situation.
- Experimental investigations, e.g. for toxicology testing, can be performed directly at Fraunhofer ITEM or are subcontracted to other testing institutes. If an external partner is needed, we can assist you in selecting an appropriate partner and in the monitoring of your studies.
- Risk assessment and expert reports: in the form of expert reports, we document the (eco)toxicological properties of substances and assess their risks to human health and the environment, for example for REACH registrations, for biocides, and for contaminations or chemical residues in foods and products.

PROJECTS

Long-term effect of modified carbon black nanoparticles on the lungs

In the joint research project NanoCOLT (grant number: BMBF 03X0153), scientists investigated the effects of carbon black nanoparticles (CBNP) after inhalation exposure, focusing in particular on the impact of different surface modifications. The project also tried to elucidate the influence of pre-existing lung tissue damage on the biological effects of CBNP. At Fraunhofer ITEM, experiments with human lung tissue slices (precision-cut lung slices) from patients with different pre-existing medical conditions were performed. Furthermore, a test system for exposing lung epithelial cells to CBNP at the air-liquid interface by using the P.R.I.T.® ExpoCube® technology was established. This system was also used to co-expose cells to CBNP and other harmful chemicals such as formaldehyde.

The results obtained in in-vitro and ex-vivo experiments were finally verified in a 90-day nose-only inhalation study in rats according to OECD guideline 413. All test systems corroborated the low toxicity level of CBNP that had already been observed in the previous project CarbonBlack. In-vitro experiments in lung epithelial cells confirmed that pre-existing cell damage induced by formaldehyde can potentiate the toxic effect of CBNP aerosols. In addition, the results of this joint research project confirmed the important impact of surface chemistry, absorption of polycylic aromatic hydrocarbons in particular, on inhalation toxicity.

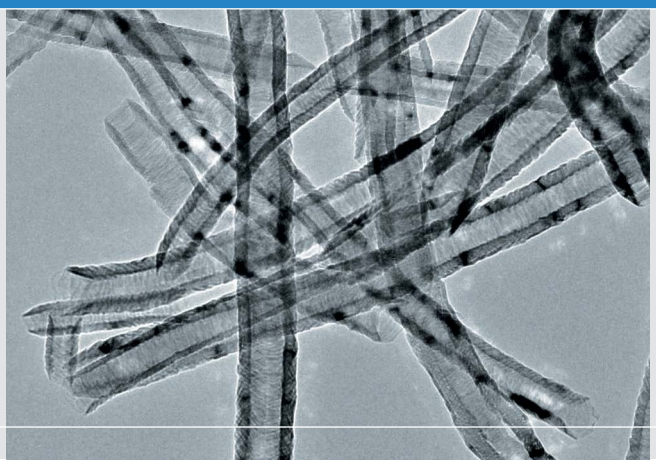
CONTACT
Dr. Tanja Hansen
Phone +49 511 5350-226
tanja.hansen@item.fraunhofer.de

Toxicological studies with nanomaterials

Over the past ten years, a focus of the traditionally intensive research on particles and fibers at Fraunhofer ITEM has been placed on synthetic nanomaterials. This trend was encouraged by the large number of new nanoscale substances that require toxicological safety testing, before they can get marketing approval. Coping with this toxicological challenge was facilitated by the knowledge gained at Fraunhofer ITEM in previous work with "ultrafine" titanium and silicon dioxide and carbon black. Compared with microparticles, studies with nanoparticles require a broader analytical spectrum, for example, with regard to their agglomeration and sedimentation behavior in liquid and air. In addition, chemical surface modifications serving technical purposes play a pivotal role when it comes to characterizing the toxic potential. The plethora of nanomaterials requires a focus to be placed on highly efficient in-vitro screening tests for cytotoxicity and genotoxicity, allowing the number of toxicologically relevant dusts to be narrowed down. Fraunhofer ITEM scientists have performed quite a few research projects exemplarily addressing the combined use of in-vitro (screening) and in-vivo tests (physiological validation). Substance classes included metal oxides (TiO_2, SiO_2, $BaSO_4$, CeO_2) and carbon compounds (e.g. different types of soot, graphenes). Because of the problems associated with fibers, a focus at present is on carbon nanotubes, as morphological features in this case have a strong impact on lung carcinogenicity.

CONTACT
Dr. Otto Creutzenberg
Phone +49 511 5350-461
otto.creutzenberg@item.fraunhofer.de

Because of the problems associated with fibers, carbon nanotubes are currently at the focus. The morphological features of this nanomaterial have a strong impact on its lung carcinogenicity.



Toxicity and selection of nonhazardous mineral fibers

Mineral fibers play an important role in our daily life. They exhibit high temperature stability and are used, for example, as insulating materials. However, since detection of the problems caused by asbestos, if not earlier, their use has been known to also pose a potential hazard to human health. Certain types of fibers trigger inflammatory reactions in the lung upon inhalation. This may cause cancer as a late effect. Critical types are inhalable, biopersistent fibers of low solubility. Besides their chemical composition, diameter and length play an important role. Fibers with a thickness > 6 µm are considered non-inhalable. In Europe fibers with a length > 20 µm are rated as possibly critical; in Germany also fibers with a length > 5 µm and a diameter < 3 µm (WHO fibers). The key aspect in the assessment is persistence of the fibers in the lung. Fibers are considered nonhazardous if their half-life in the lung is below 40 days. Fraunhofer ITEM offers performance of the fiber biopersistence test allowing the half-life of mineral fibers after intratracheal administration to be determined. This test is a prerequisite for marketing authorization. Applications for certification of such fibers to enable marketing authorization can be filed with EUCEB (EUropean CErtification Board for mineral wool products) for the whole of Europe or with Gütegemeinschaft Mineralwolle (GGM) for Germany.

CONTACT
Dr. Roman Halter
Phone +49 511 5350-521
roman.halter@item.fraunhofer.de

Five years of Biocidal Products Regulation – what has changed?

The Biocidal Products Regulation (BPR 528/2012) became effective in 2013. The BPR aims to harmonize the EU market and to simplify the approval of biocidal active substances and authorization of biocidal products, while ensuring a high level of protection for humans and the environment. Especially in the past five years of BPR, many technical, regulatory, and scientific improvements have been released: The "Union Authorization" is an attractive alternative enabling an EU-wide authorization in one step. Furthermore, biocidal products containing the same active substances and which are used for similar purposes can be authorized as a "biocidal product family". Identical products can be registered more easily as "same biocidal product". As technical improvements, several new or updated IT tools simplify data management, submission of dossiers, and communication between the applicant and the authorities. All these improvements with their chances but also limitations pose a big challenge for industry. Fraunhofer ITEM supports its clients in scientific and regulatory issues. This comprises evaluation of all data, assessment of potential substances of concern, dossier preparation and submission. The scientific expertise also includes approaches to solve difficult analytical problems and to address issues in non-standard toxicology such as the development of integrated testing strategies and new approach methodologies (NAMs), e.g. read-across and in-vitro approaches.

CONTACT
Ariane Zwintscher
Phone +49 511 5350-312
ariane.zwintscher@item.fraunhofer.de

Test battery to evaluate acute inhalation toxicity prior to OECD 403 studies

New plant protection products are tested for inhalation toxicity according to OECD guideline 403. With a view to reducing the number of animals and amount of test substance required, the present project aimed to implement ex-vivo and in-vitro screening tests that can be used to evaluate acute inhalation toxicity prior to OECD 403 studies. Mancozeb and chlorothalonil, two reference compounds of known toxicity, were tested with complementary methods: the isolated perfused rat lung (IPL) model and a human lung epithelial cell line that was used with the Fraunhofer-patented P.R.I.T.® ALI technology. The PreciseInhale® technology enabled efficient aerosol generation. Lung viability in the IPL experiments was determined by means of the respiratory parameters tidal volume, resistance, dynamic lung compliance, and relative increase in lung weight. Cell viability was determined in the in-vitro assay. Exposure of IPLs to the test items led to moderate changes in the monitored respiratory parameters, but also resulted in a dose-dependent increase in lung weight and thus in lung edema. The in-vitro exposure led to a dose-dependent reduction of viability. Both tests showed a significantly lower toxic potential for mancozeb than for chlorothalonil, thereby confirming the results of the in-vivo studies. In the next step, further substances are planned to be tested to confirm the predictive value of the test battery.

CONTACT
Dr. Jan Knebel
Phone +49 511 5350-273
jan.knebel@item.fraunhofer.de

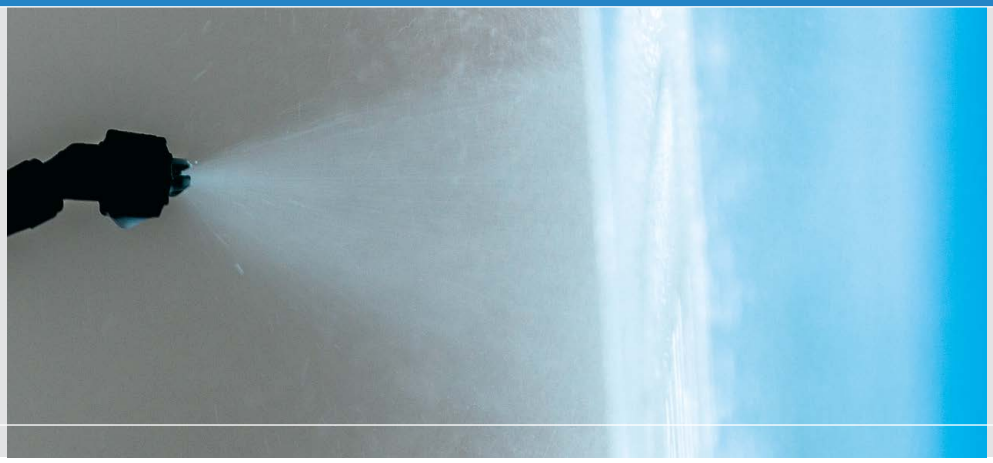
ECETOC TRA – assessing inhalation and dermal exposure during spraying activities

For the registration process under REACH chemical safety assessments need to be provided. The ECETOC TRA tool is a tier-1 model for estimating environmental exposure as well as dermal and inhalation exposure of professional users and consumers. For several process categories (PROCs), this tool has been demonstrated to provide conservative estimates for occupational exposure. For the two process categories "industrial spraying" (PROC 7) and "professional spraying" (PROC 11), however, a mismatch between model and field data has been indicated. For some situations, the exposure estimates provided by ECETOC TRA are not conservative enough to allow reliable risk assessment regarding the inhalation exposure of workers during PROC 7 and PROC 11 activities*. In a project funded by the European Chemical Industry Council (CEFIC), Fraunhofer ITEM scientists and members of the European Solvents Industry Group (ESIG) have joined forces to shed more light on the performance of the ECETOC TRA tool regarding PROC 7 and PROC 11 activities. For this purpose, inhalation (aerosol and gas phases) and dermal exposure data will be generated in a series of simulation scenarios covering the most prominent features of spraying activities. The focus of the investigations is on a vapor pressure-dependent shift in the release rates of the aerosol and gas phases.

CONTACT
Katharina Blümlein Ph.D.
Phone +49 511 5350-213
katharina.bluemlein@item.fraunhofer.de

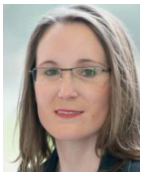
* BAuA F2303: Final Overall Project Summary Report (2015).
Kupczewska-Dobecka, M. et al.: Int J Occup Med Environ Health. 24 (2): 208-217 (2011).
Hofstetter, E. et al.: Ann Occup Hyg, 57 (2): 210-220 (2013).

The aim of a study is to generate comprehensive data on inhalation and dermal exposure during foam spraying compared with droplet spraying of biocidal products.



Aerosol release during application of biocidal foam products

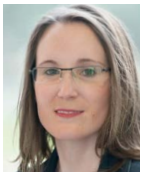
Application of biocides in the form of foam sprays is increasing, for example, for large-surface disinfection in food processing areas or for biocidal pest control. For the alternative droplet spraying method, comprehensive data sets on inhalation and dermal exposure are available and established exposure assessment models exist; however, this information is lacking for the foam spraying method. In an investigation performed earlier on behalf of the German Federal Institute for Occupational Safety and Health (BAuA), a small number of qualitative measurements was carried out, suggesting that foam spraying also causes aerosol release, but apparently in lower quantities than droplet spraying. Fraunhofer ITEM and the Institute of Occupational, Social and Environmental Medicine of the University of Erlangen-Nuremberg are collaborating in a project commissioned by BAuA, aimed at generating comprehensive data on inhalation and dermal exposure during foam spraying compared with droplet spraying. A special focus is on quantifying the exposure reduction during foam spraying compared with traditional droplet spraying processes. In addition, the data shall support the development of a corresponding exposure model. To this end, Fraunhofer ITEM scientists are conducting comprehensive model experiments. The results will subsequently be verified by means of workplace measurements.



CONTACT
Dr.-Ing. Katharina Schwarz
Phone +49 511 5350-139
katharina.schwarz@item.fraunhofer.de

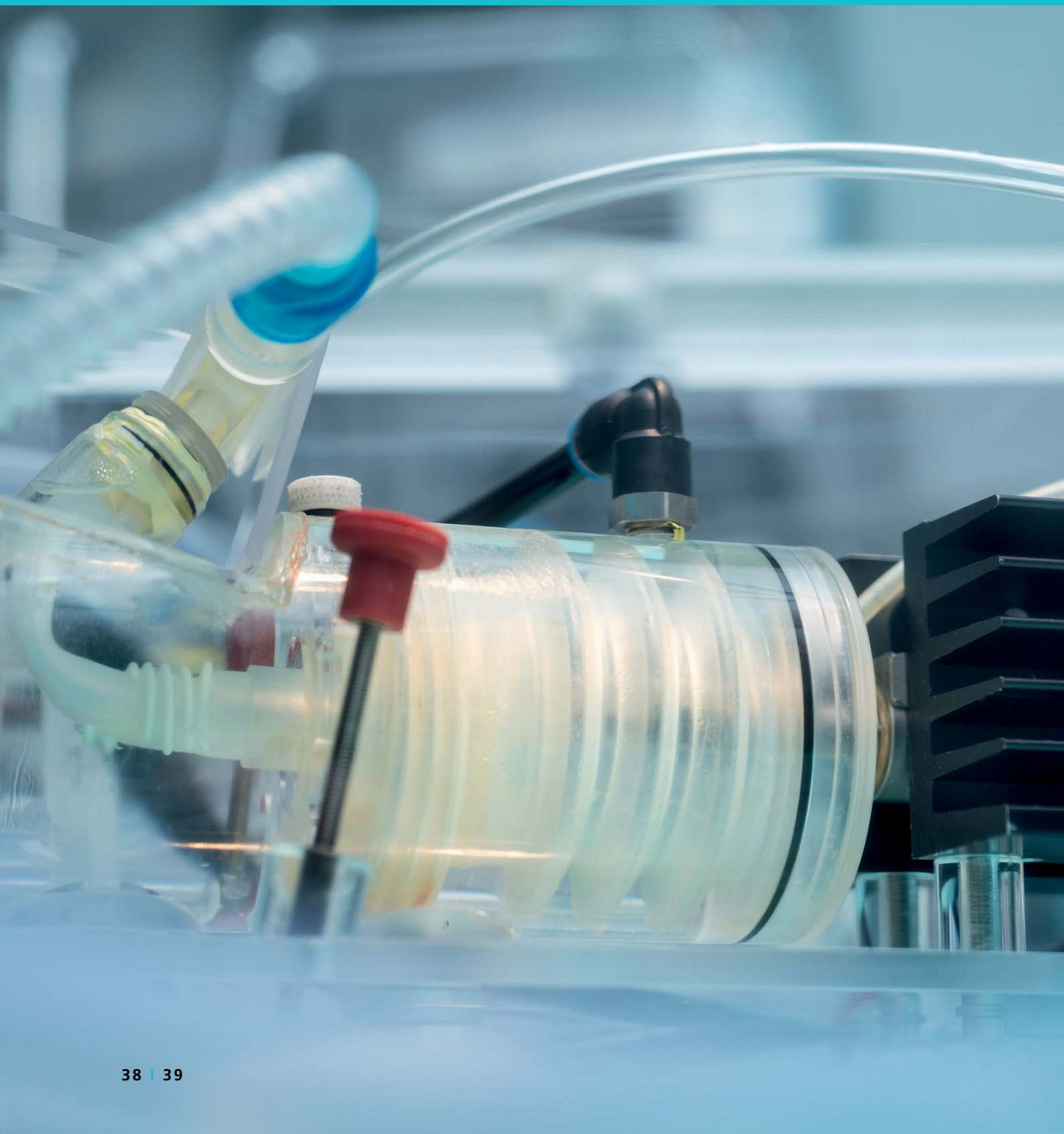
Determination of thoracic and respirable aerosol fractions of spray products

Fraunhofer ITEM scientists have developed a versatile and simple mass balance method to measure the release fractions of thoracic and respirable particles from non-volatile compounds of spray products. The release fractions are defined as the ratio between the mass of suspended non-volatile particulate matter in the thoracic and respirable particle size ranges and the total mass of non-volatile material released with the spray action. For the measurement, a spray bolus of short duration and of defined mass is sprayed into a well stirred control chamber. The respirable and thoracic aerosol mass associated with the spray bolus is then determined by measuring the time-averaged mass concentration inside the control volume and the halftime of the exponential concentration decrease to be expected in well stirred systems to correct for mass losses during sampling. The method can be used for a wide range of spray products and technologies for which the release fractions vary by orders of magnitude. A simple rule of thumb was derived from the data, allowing the release fractions to be estimated based on a characteristic diameter of the spray droplets. The mass balance method can be used for substance classification as well as for generating input data for exposure assessment and indoor air quality modeling.



CONTACT
Dr.-Ing. Katharina Schwarz
Phone +49 511 5350-139
katharina.schwarz@item.fraunhofer.de

TRANSLATIONAL BIOMEDICAL ENGINEERING



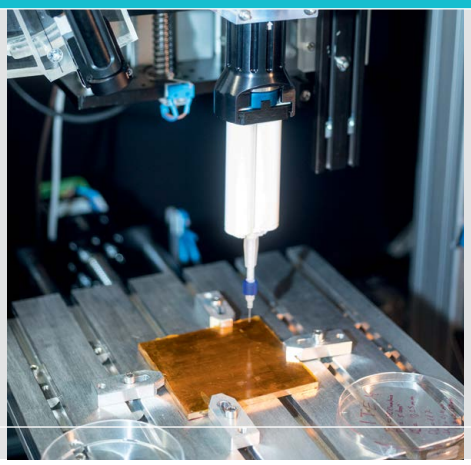
OUR SERVICES: FROM IDEA TO SAFE MEDICAL DEVICE

Development of medical devices is a complex process taking place in a highly regulated environment. Besides specific technical expertise in this area, compliance with the relevant regulatory requirements is of pivotal importance. In this environment, we conduct research, development projects, and device testing, based on several years of experience in the development of medical devices.

Close dovetailing with the institute's other working groups with scientific or medical focuses allows the team to provide comprehensive support to clients in their development projects, to the point of performing the required preclinical and early-phase clinical studies. Cooperation within the High-Performance Center Translational Biomedical Engineering and with external development partners from industry and academia enables flexible responses to project-specific requirements. In the area of quality and risk management, we support qualification of external technology processes.

One focus is on implants: We develop tailored methods for safety and functionality testing of implants (in compliance with EN ISO 14791 and ISO 10993) and new accelerated aging models for polymer implants in particular. The second focus is on conducting and assisting the development of novel technologies for administration of medicinal aerosols towards smart drug/device combination products.

The services offered by Fraunhofer ITEM assist you on the way from idea to safe medical device.



Device development and processes suitable for SMEs

Our conceptual development work is reflected in the development of medical devices and test benches. Development of devices is performed either as contract research or supporting other research projects. Whenever required, new test benches are developed in parallel and are made available for testing of newly developed devices. This allows our clients to substantially reduce the obstacles encountered during development of innovative products and the risk of technology transfer failure. Furthermore, within our network we provide biomedical engineering systems for demonstration purposes and prototypes for clinical trials.

Development of implants: Fraunhofer ITEM scientists are developing test methods to determine the long-term behavior of polymer implants that exceed the known standards of temperature acceleration. Such research is geared towards preventing repeat surgery wherever possible and towards minimizing the risk of implant failure.

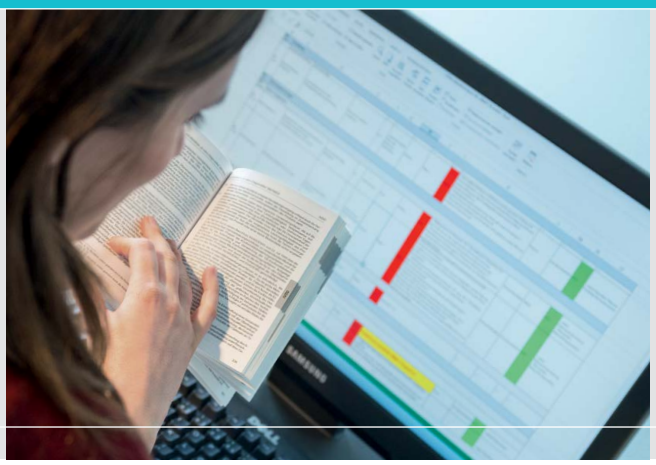
Development of medical inhalers: Medical inhaler technology is increasingly evolving from simple, constant drug administration to intelligent, breathing-controlled systems for inhalation treatment with pharmaceuticals. At Fraunhofer ITEM, we develop products and test benches to the point of meeting the requirements for use in first clinical trials or as validated measurement systems. We are thus able to make an important contribution to your development process: from initial explorative research via prototype manufacturing and verification to the first clinical trials. Our aim is to support above all small and medium-sized enterprises in their development projects.

Testing and testing scenarios

Besides the use of standard methods, a focus here is on the development of novel test methods. These include above all in-vitro accelerated aging models for implants, which are necessary to allow stability testing of such implants that can be expected to be of long-term durability, within a short time span.

The test systems for medical devices intended for use in aerosol and inhalation therapy follow a risk management approach – the relevant standards such as ISO 20072 do not stipulate the application of particular test methods. For example, when it comes to testing novel inhalers for use in neonates, there is a need to develop new test methods, as there are no suitable test systems available.

Testing of implants: Modern implants are basically designed for early childhood implantation and 100-year periods of use. In order to ensure compliance with these requirements already during development, accelerated testing must be employed. Whilst exposure to higher temperatures has been a working solution for many applications, thin-film polymer devices face reliability limits with a pure temperature increase. To solve this problem nonetheless, we develop new test methods that make use of a multi-parameter model with elevated pressure and artificial body fluids at high concentrations. By setting up mathematical modeling in parallel, we are able to additionally substantiate the desired long-term life span forecasts.



Testing of medical inhalers: Testing of novel devices with standard methods is often not possible. This is why relevant standards leave scope for action. ISO 20072, for example, does not stipulate the test method to be used for testing of inhalation devices. Quite the contrary, for novel inhalation systems in many cases it is necessary to follow a risk-based approach and adapt existing or develop new test methods. We use standard methods as well, but our focus is on testing novel devices and especially devices used in inhalation circuits for adults and neonates. This includes not only measurements of device performance, but also investigation of any impact the delivered substance may have on the whole ventilator circuit. This might be, for example, blockage of filters or other air-conducting pathways, such as nasal prongs of neonates.

Safety and risk assessment of medical devices

The clinical use of medical devices requires that this use poses no risk to the safety and health of patients and device users. Consequently, risk management plays a pivotal role in the development of medical devices. Based on our experience, we support our partners throughout the development phase in minimizing any risks in compliance with the relevant standards. We support our partners with our expertise in the development and implementation of safety features, the formal implementation of risk management, and any risk mitigation measures that may be required.

Regulatory support to reach marke approval of medical devices

An important pillar for success in the development of medical device technology is the regulatory strategy. The earlier this strategy is established, the shorter the time to market. We offer support with relevant regulatory issues already in the initial phases of product development, especially to small enterprises and startups. This support includes assistance in the selection of an approval strategy, implementation of this strategy, and workshops to sensitize for processes and documentation necessary for market approval. This is particularly important, given that the currently still valid Medical Device Directive will soon be replaced by the much more stringent EU-wide Medical Device Regulation.

PROJECTS

System developed for inhaled drug administration to preterm and newborn babies

Because of the lacking coordination capacities of very young patients and the changes in lung anatomy and breathing mechanics throughout childhood, inhaled drug administration to infants, babies, and preterm neonates in particular requires the development of automated systems that are able to adapt to the individual situation. Sensory in-situ breath monitoring and adjustment of the administered dose have to be coupled even more closely here than in adult patients. For example, there is yet no breath-synchronized drug delivery system available that would enable efficient and safe administration of inhalation therapeutics to preterm infants. Given the special physiology of preterm neonates – very small tidal volume of 4 to 6 ml/kg, high breathing rate of 40 to 60 breaths per minute, short inhalation duration of 0.25 to 0.4 seconds, and spontaneous breathing (constantly changing parameters) – and, in relation to the small tidal volume, the rather large distance between nebulizer and patient interface (e.g. nasal prong), the currently available systems are hardly suitable. Furthermore, current breath triggering systems either depend on the breathing signal measured in the ventilation tube or are electrically coupled to a potential ventilation system. This last variant in particular represents a change to a registered medical device, resulting, in principle, in the registration becoming ineffective and consequently posing a substantial regulatory hurdle.

This is why scientists of Fraunhofer ITEM and TU Braunschweig have developed a stand-alone system that makes use of a sensor film (TU Braunschweig, Institute for Microtechnology) for breath detection. The sensor film measures the expansion of the patient's chest resulting from respiratory movements. Based on the recorded signals, an algorithm determines the inspiratory and expiratory phases in advance. Via a special miniaturized aerosol valve with ultra-short response times integrated into a nasal prong, the aerosol is released just in time as a bolus directly into the patient's nose.

Such a system, for the first time ever designed for preterm infants and newborn babies, enables precise dose control and a significant increase in administration efficacy. Among other benefits, treatment times can thus be reduced. Furthermore, temporal variation of bolus delivery allows either more central (drug delivery at the end of the inhalation) or more peripheral lung areas (drug delivery at the beginning of the inhalation) to be treated. This enables targeted local aerosol deposition in specific lung areas.

The system has been designed such that the components getting in contact with patients are low-cost and easy to produce. They can thus be used as disposables for reasons of hygiene.

CONTACT
Dr. Gerhard Pohlmann
Phone +49 511 5350-116
gerhard.pohlmann@item.fraunhofer.de

For improved hearing: an implant that will curl autonomously once inserted into the cochlea reduces the distance between the nerve cells in the cochlea to be stimulated and the stimulating electrodes of the implant.

Efficient medical device prototyping

In October 2017, the project TransPlaMed (translational manufacturing platform for innovative medical devices) was launched at Fraunhofer ITEM – a collaborative project with Fraunhofer IST, the University of Applied Sciences and Arts in Göttingen, TU Braunschweig, the Lower Saxony Center for Biomedical Engineering, Implant Research and Development (NIFE) and Blackrock Microsystems Europe GmbH. Manufacturing of state-of-the-art medical devices requires special technologies. These are available in the German life science triangle Göttingen-Braunschweig-Hannover, however, they often do not meet the regulatory requirements for the manufacturing of medical device prototypes. The aim of the TransPlaMed project, therefore, is to integrate these external processes into an overall quality and risk management strategy. By working out a resource-efficient platform strategy, the scientists want to prove that distributed manufacturing of medical device prototypes as part of conformity evaluation can be realized efficiently and in compliance with regulatory requirements. They want to provide the proof of concept based on an implant design (provided by Blackrock Microsystems Europe) conceived to enable more precise monitoring of patients' brain activities, e.g. in epilepsy, to improve targeted treatment. Besides prototype manufacturing, the project will also address economic issues and safety aspects of data exchange to cover the challenges of distributed manufacturing in their entirety.

CONTACT
Jelena Pankalla
Phone +49 511 5350-234
jelena.raisa.pankalla@item.fraunhofer.de

Self-curling cochlear implant for improved hearing

The High-Performance Center Translational Biomedical Engineering allows Fraunhofer ITEM, in cooperation with the Biomaterial Engineering group at the Hannover Medical School, to take innovations directly into translational research. At present, the focus is on improving cochlear implants. They represent the most successful category of electric implants, however, while they allow hearing restoration in many patients, application of these implants is not optimal yet. This becomes manifest in particular in situations where several people speak simultaneously or where there is strong ambient noise, for example, during social events, conferences, or at workplaces. A major problem is the large distance between the nerve cells in the cochlea that are to be stimulated and the stimulating electrodes of the implant. This distance is due to the insertion procedure itself: The nerve cells are located on the inner curve of the helical cochlea, whereas the implant has to be inserted along its outer curve. Striving to improve this weak point, scientists have now developed an implant that will curl autonomously once inserted into the cochlea. Key to this development was a special mixture of hydrogel and silicone, enabling the intended swelling and providing at the same time a matrix for the swelling process. The mission of the High-Performance Center Translational Biomedical Engineering now is to evaluate the long-term stability and biocompatibility of these self-curling implants and take them to market with industry partners to make them available to patients.

CONTACT
Prof. Dr. Theodor Doll
Phone +49 511 5350-248
theodor.doll@item.fraunhofer.de

PERSONALIZED TUMOR THERAPY

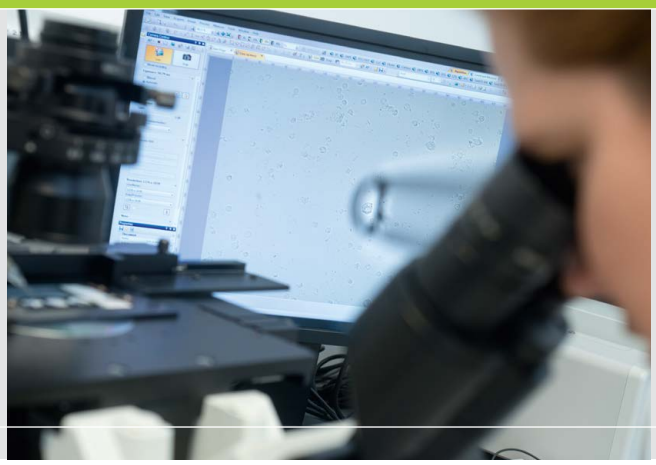
OUR SERVICES: FROM MOLECULAR ANALYSIS TO PERSONALIZED THERAPY

The institute's Regensburg-based Division of Personalized Tumor Therapy is committed to doing research on metastatic disease, to understanding a patient's individual condition, to establishing appropriate diagnostics, and to advancing prevention and therapy optimization.

We have special expertise in the comprehensive characterization of circulating or disseminated cancer cells. These can be collected as circulating tumor cells (CTCs) by taking ordinary blood samples (also referred to as "liquid biopsy") from patients, or they can be isolated from lymph node tissue or bone marrow as disseminated cancer cells (DCCs). Our expertise also includes the analysis of cell-free, tumor-derived blood components (circulating tumor-DNA, microvesicles) and innovative tissue-based analytical methods (tissue biopsy). A tissue bank with corresponding logistics for sample storage is being set up.

With our expert knowledge in the fields of "Cellular and molecular diagnostics", "Innovative molecular technologies and biomarker discovery", "Preclinical therapy models", "Disease modeling", and "High-throughput drug and target discovery", we work on a broad variety of topics in the fields of liquid biopsy and rare cell populations. Our in-house data management and comprehensive bioinformatics enable custom-fit analyses of the generated data. The Division of Personalized Tumor Therapy has been certified by TÜV Süd according to DIN ISO 9001:2015 and thus complies with international standards.

The services offered by this division can assist you on the way from molecular analysis to personalized tumor therapy.



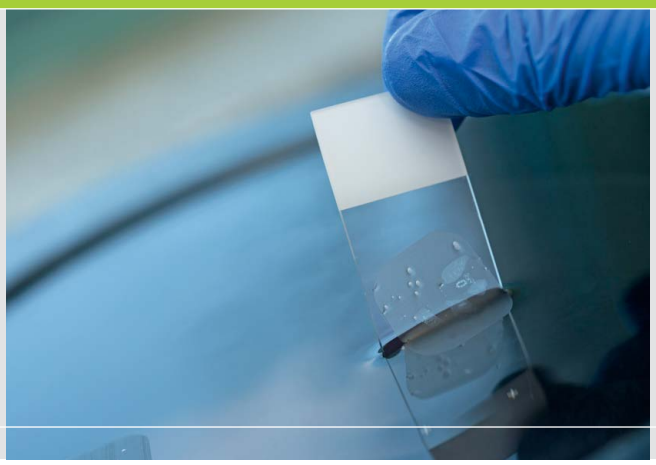
Single-cell analysis

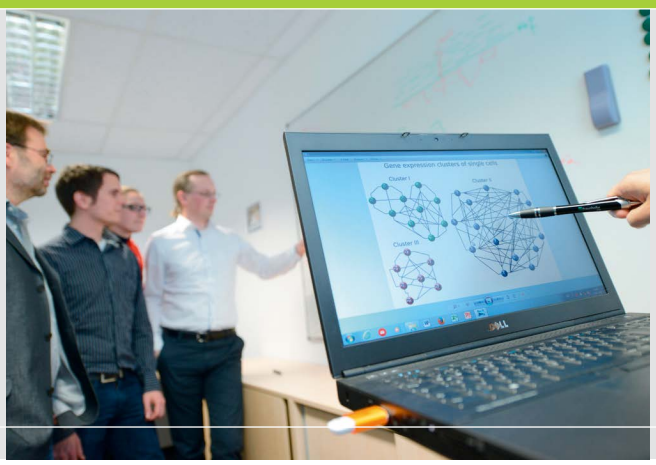
Enrichment, isolation and molecular analysis of rare cells

Our commitment is to drive innovative therapeutic approaches by decoding the underlying mechanisms in complex diseases on a single-cell level. The focus is on solid cancers, e.g. the analysis of circulating tumor cells (CTCs) and disseminated cancer cells (DCCs), however, our technologies can be adjusted to different application areas, such as stem cell therapy. Our expertise ranges from the development and implementation of individual enrichment and staining strategies to the isolation of pure cell populations, down to a single target cell. As an accredited single-cell laboratory and through our cooperation with the University of Regensburg, we have access to a sample biobank generated from single CTCs/DCCs of patients with different cancer types. We use these for biomarker research and target validation, and for many samples a correlation with the clinical follow-up can be established. We thus work in a perfect environment for translational research within clinical studies.

Decoding of single cells

For the development of tailored solutions for single-cell or rare-cell analysis, we offer expert knowledge in next-generation sequencing (NGS) and microarray technologies, in particular at the single-cell DNA and RNA levels. Our in-house developed workflows are optimized for the analysis of clinical low-input or single-cell samples, e.g. cancer cells isolated from body fluids, fine-needle aspirates and tissue specimens. Our workflow integrates quality control assays for optimal sample selection, technical implementation, and bioinformatics evaluation.





Innovative tumor models

In-vitro and in-vivo drug testing

For efficacy testing of drugs in innovative preclinical models representing systemic cancer disease, we offer experience in the generation of cellular models for functional analysis of rare cancer cell populations from fluids, organs, and primary tumors. To this end, we have established technologies allowing expansion of few DCCs or CTCs despite their extremely low abundance. Such preclinical models allow us to perform individualized pharmaceutical drug tests, both in vitro and in vivo, and provide the opportunity to comparatively test drugs on cancer subpopulations.

Advanced preclinical PDX models

Preclinical animal models only partially represent the patient situation. Fraunhofer ITEM in Regensburg is developing optimized PDX (patient-derived xenograft) models allowing more representative preclinical drug testing. Our advanced models are based on patient-derived metastatic precursor cells (DTCs) or circulating tumor cells (CTCs). In addition, we concomitantly generate a human immune system in these models, which infiltrates the human tumors and develops phenotypes (e.g. tumor-associated macrophages) that have been described in patient samples. This allows both the tumor development and the dissemination of cancer cells into different organs to be followed in the presence of human immune cells. Our services include development of individualized preclinical in-vivo models to test in particular immunomodulatory drugs on target cells of systemic disease.

Mathematical modeling and bioinformatics

Multi-level disease modeling

Data analysis and biological process modeling are necessary to facilitate development of innovative therapies and support their clinical application. Therefore, we offer our clients profound data analysis and result visualization as well as aim-oriented mathematical modeling of biological mechanisms, disease progression, and therapeutic effects. We can also assist in experimental planning and statistical evaluation of experiments and patient trials. Our spectrum of methods ranges from feature selection, pattern recognition, machine learning, and network analysis to population dynamics, probability theory, and predictive modeling.

Bioinformatics services

Complex biological questions normally cannot be addressed by generalized "one-fits-all" approaches. Our commitment is to provide tailored bioinformatics solutions that provide a comprehensive yet specific answer to your experimental questions. We offer our clients expertise in bioinformatic analysis of high-throughput data from next-generation sequencing or microarray experiments. The Fraunhofer ITEM bioinformatics experts in Regensburg are focused on analyzing human single-cell omics data. Our expertise ranges from simple gene expression via complex genome reconstruction analyses to the development of novel algorithms and applications. Clients are invited to use our counseling services.

PROJECTS

Semi-automated diagnostics for disseminated melanoma cells

Besides the size of the primary tumor and the presence or absence of metastasis, another criterion in the staging of malignant tumors is lymph node colonization. When assessing the prognosis of a patient with malignant melanoma, the status of the so-called sentinel lymph node is currently considered the most important factor. Detection even of very small cell nests or single tumor cells will have an impact on the therapy decision and has, therefore, been included in the AJCC (American Joint Committee on Cancer) staging system. Standardized methods for determination of the minimum tumor burden, however, are still lacking. Molecular characterization of disseminated tumor cells in addition can provide important patient-specific clues to the efficacy of treatment options.

This is why the Working Group on Cellular and Molecular Diagnostics of the Fraunhofer ITEM Division of Personalized Tumor Therapy has collaborated with the University Hospital Regensburg, establishing a semi-automated workflow to systematically detect disseminated melanoma cells in sentinel lymph nodes and isolate these for downstream molecular analyses. Lymph node tissue is first disaggregated and purified to a single-cell suspension. Potential tumor cells are then fluorescence-stained by using two markers that are highly specific of malignant melanoma (MCSP and gp100). After depletion of immune cells that are also present in the lymph node, the tumor cells are captured via dielectric pulses using the semi-automated DEPArray™ technology and are systematically isolated. During this process, all cells are measured and precisely documented by means of the integrated microscope with camera. Different selection parameters enable detailed comparison of the individual cells with regard to staining and morphological criteria.

To enable downstream molecular analyses of the isolated tumor cells global amplification of single-cell genomes is performed by using a special method (*Ampli*1™) developed by the two collaborating institutions. This allows the DNA of isolated single tumor cells to be investigated, for example, for disease-specific point mutations or typical chromosomal alterations. In validation experiments for this workflow, the scientists isolated a total of 201 single cells from 20 lymph nodes and were able to identify melanoma-specific point mutations in cells from six lymph nodes. Furthermore, a new method for assessing chromosomal integrity that is not yet commercially available was successfully tested on these single-cell samples.

Thanks to the development of this semi-automated workflow for the detection and isolation of single disseminated melanoma cells in sentinel lymph nodes, a standardized method is now available for reliable detection of the clinically relevant minimum tumor burden and further analysis of relevant factors for treatment decisions. This makes it possible to apply a targeted and personalized treatment to melanoma patients whose tumor cells have already disseminated to the sentinel lymph node.

CONTACT
Dr. Barbara Alberter
Phone +49 941 298480-25
barbara.alberter@item.fraunhofer.de

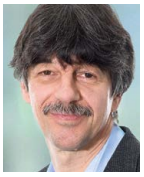
Whole-exome sequencing allows the complete mutational landscape in cancer to be determined at the single-nucleotide level.

Highly reliable single-cell whole-exome sequencing of circulating tumor cells

Whole-exome sequencing (WXS), which means sequencing of all the protein-coding regions of the human genome, allows the complete mutational landscape in cancer to be determined at the single-nucleotide level. Together with whole-genome amplification methods for single tumor cells, the full potential of this method can be applied down to the single-cell level to investigate the heterogeneity in an individual's disease.

To enable whole-genome sequencing of single tumor cells from metastasic breast cancer patients, circulating tumor cells (CTCs) were first collected from these patients by means of blood samples (also referred to as "liquid biopsy"). In the following, the *Ampli*1™ WGA method for single-cell whole-genome amplification was combined with the whole-exome enrichment technology SureSelect XT. This approach was selected for several reasons: (1) The *Ampli*1™ WGA technology excludes random priming, thereby preventing priming-derived sequence alterations from being mistaken for real. (2) The deterministic nature of this technology ensures that the genomic amplicon population is amplified equally in all single cells of all patients, thus facilitating implementation of sample quality control. And (3) Agilent SureSelect XT has shown the best performance in coverage of clinically interesting mutations. The combination of both technologies was optimized by means of *Ampli*1™ WGA samples derived from single peripheral blood lymphocytes (PBLs) isolated from a healthy human donor. The optimized workflow turned out to yield highly reproducible and reliable results that are almost equivalent to those of routine diagnostic pathology.

More than 80 percent of all reads mapped with high confidence could be defined as "on target", addressing DNA segments from the target regions of WXS. Of the total sequence content defined in the target regions, 74.8 percent were addressed by at least 11 independent reads. Applying the established approach to single-cell CTCs of metastatic breast cancer patients from the multi-center phase-III study DETECT III, the newly developed sample quality control enabled not only identification of high-quality amplified CTC samples, but also reliable prediction of their performance in downstream WXS. Comparison of the identified mutation profiles with corresponding PBLs allowed amplification-induced sequence alterations to be ruled out; however, an unexpectedly high genomic plasticity of PBLs also became apparent. Development of a bioinformatics tool fine-tuned for the *Ampli*1™ WGA technology will allow single-cell WXS data sets to be used for reliable copy number variation (CNV) analyses in addition to mutation analyses, thus enabling a more comprehensive picture of genomic variations in single CTCs to be drawn.



CONTACT
Dr. Stefan Kirsch
Phone +49 941 298480-26
stefan.kirsch@item.fraunhofer.de

CONTACTS

Fraunhofer ITEM has pooled the competencies from its various divisions in three business units: Drug Development, Chemical Safety and Assessment, and Translational Biomedical Engineering. Another focus is on personalized tumor therapy, a subject area explored by the scientists of the corresponding Regensburg-based division of Fraunhofer ITEM. Below please find the contacts for the different thematic areas and services offered. Please do not hesitate to contact these persons directly, should you have any questions or needs.

Institute directors

Prof. Dr. med. Norbert Krug
Director
Medical Director
Phone +49 511 5350-8100
norbert.krug@item.fraunhofer.de

Prof. Dr. med. Jens Hohlfeld
(Deputy Director)
Division Director of Airway Research
Phone +49 511 5350-8101
jens.hohlfeld@item.fraunhofer.de

Drug Development

Dr. rer. nat. Holger Ziehr
Coordinator of the business unit Drug Development
Division Director of Pharmaceutical Biotechnology
Fraunhofer ITEM, Braunschweig
Phone +49 531 6181-6000
holger.ziehr@item.fraunhofer.de

Dr. rer. nat. Henning Weigt
Coordinator of the business unit Drug Development
Expert Group Manager Regulatory Research and Support
Phone +49 511 5350-329
henning.weigt@item.fraunhofer.de

Development and manufacturing of active biopharmaceutical ingredients

Dr. rer. nat. Holger Ziehr
Division Director of Pharmaceutical Biotechnology
Coordinator of the business unit Drug Development
Fraunhofer ITEM, Braunschweig
Phone +49 531 6181-6000
holger.ziehr@item.fraunhofer.de

Regulatory research and risk assessment of pharmaceuticals

Dr. rer. nat. Henning Weigt
Expert Group Manager Regulatory Research and Support
Coordinator of the business unit Drug Development
Phone +49 511 5350-329
henning.weigt@item.fraunhofer.de

Preclinical testing

Prof. Dr. rer. nat. Armin Braun
Division Director of Preclinical Pharmacology
Phone +49 511 5350-263
armin.braun@item.fraunhofer.de

Clinical trials

Prof. Dr. med. Jens Hohlfeld
Division Director of Airway Research
Phone +49 511 5350-8101
jens.hohlfeld@item.fraunhofer.de

Dr. med. Dipl.-Kfm. Philipp Badorrek
Department Head of Clinical Airway Research
Phone +49 511 5350-8130
philipp.badorrek@item.fraunhofer.de

Chemical Safety and Assessment

Dr. rer. nat. Annette Bitsch
Coordinator of the business unit Chemical Safety and Assessment
Division Director of Chemical Risk Assessment, Databases and Expert Systems
Phone +49 511 5350-302
annette.bitsch@item.fraunhofer.de

Dirk Schaudien Ph.D.
Coordinator of the business unit Chemical Safety and Assessment
Department of Pathology
Phone +49 511 5350-324
dirk.schaudien@item.fraunhofer.de

Katharina Blümlein Ph.D.
Coordinator of the business unit Chemical Safety and Assessment
Department of Environmental and Bioanalytics
Phone +49 511 5350-213
katharina.bluemlein@item.fraunhofer.de

Development of test methods and analytical procedures

Dr. rer. nat. Sven Schuchardt
Department Head of Environmental and Bioanalytics
Phone +49 511 5350-218
sven.schuchardt@item.fraunhofer.de

Toxicology testing of chemical substances

Prof. Dr. med. vet. Clemens Dasenbrock
Division Director of Toxicology and Environmental Hygiene
Phone +49 511 5350-408
clemens.dasenbrock@item.fraunhofer.de

Translational Biomedical Engineering

Exposure characterization

Dr.-Ing. Katharina Schwarz
Department of Aerosol Technology
Phone +49 511 5350-139
katharina.schwarz@item.fraunhofer.de

Dr. rer. nat. Stefan Hahn
Group Manager of Exposure Assessment
Phone +49 511 5350-326
stefan.hahn@item.fraunhofer.de

Regulatory research and risk assessment of chemicals

Dr. rer. nat. Annette Bitsch
Division Director of Chemical Risk Assessment, Databases and Expert Systems
Phone +49 511 5350-302
annette.bitsch@item.fraunhofer.de

Dr. rer. nat. Oliver Licht
Division of Chemical Risk Assessment
Phone +49 511 5350-334
oliver.licht@item.fraunhofer.de

Dr. rer. nat. Gerhard Pohlmann
Coordinator of the business unit Translational Biomedical Engineering
Division Director of Translational Biomedical Engineering
Phone +49 511 5350-116
gerhard.pohlmann@item.fraunhofer.de

Prof. Dr.-Ing. Theodor Doll
Coordinator of the business unit Translational Biomedical Engineering
Head of the High-Performance Center Translational Biomedical Engineering
Phone +49 511 5350-230
theodor.doll@item.fraunhofer.de

Dr. Pohlmann and Prof. Doll are also your contacts for the following subject areas:

Device development and processes suitable for SMEs

Testing and testing scenarios

Safety and risk assessment of medical devices

Regulatory support for market approval of medical devices

Personalized Tumor Therapy

Prof. Dr. med. Christoph Andreas Klein
Division Director of Personalized Tumor Therapy
Manager of the Working Group on Disease Modeling
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-55
christoph.andreas.klein@item.fraunhofer.de

Dr. med. Bernhard Polzer
Manager of the Working Group on Cellular and Molecular Diagnostics
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-23
bernhard.michael.polzer@item.fraunhofer.de

Single-cell analysis

Dr. rer. nat. Stefan Kirsch
Manager of the Working Group on Innovative Molecular Technologies and Biomarker Discovery
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-26
stefan.kirsch@item.fraunhofer.de

Prof. Dr. med. Christoph Andreas Klein
Manager of the Working Group on Disease Modeling
Division Director of Personalized Tumor Therapy
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-55
christoph.andreas.klein@item.fraunhofer.de

Dr. med. Bernhard Polzer
Manager of the Working Group on Cellular and Molecular Diagnostics
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-23
bernhard.michael.polzer@item.fraunhofer.de

Innovative tumor models

Dr. rer. nat. Christian Werno
Manager of the Working Group on Preclinical Therapy Models
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-51
christian.werno@item.fraunhofer.de

Mathematical modeling and bioinformatics

Dr. rer. nat. Martin Hoffmann
Working Group on Disease Modeling
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-28
martin.hoffmann@item.fraunhofer.de

Dr. rer. nat. Urs Lahrmann
Working Group on Innovative Molecular Technologies and Biomarker Discovery
Fraunhofer ITEM, Regensburg
Phone +49 941 298480-29
urs.lahrmann@item.fraunhofer.de

FRAUNHOFER-GESELLSCHAFT

Research of practical utility lies at the heart of all activities pursued by the Fraunhofer-Gesellschaft. Founded in 1949, the research organization undertakes applied research that drives economic development and serves the wider benefit of society. Its services are solicited by customers and contractual partners in industry, the service sector and public administration.

At present, the Fraunhofer-Gesellschaft maintains 72 institutes and research units. The majority of the more than 25,000 staff are qualified scientists and engineers, who work with an annual research budget of 2.3 billion euros. Of this sum, almost 2 billion euros is generated through contract research. Around 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Around 30 percent is contributed by the German federal and state governments in the form of base funding, enabling the institutes to work ahead on solutions to problems that will not become acutely relevant to industry and society until five or ten years from now.

International collaborations with excellent research partners and innovative companies around the world ensure direct access to regions of the greatest importance to present and future scientific progress and economic development.

With its clearly defined mission of application-oriented research and its focus on key technologies of relevance to the future, the Fraunhofer-Gesellschaft plays a prominent role in the German and European innovation process. Applied research has a knock-on effect that extends beyond the direct benefits perceived by the customer: Through their research and development work, the Fraunhofer Institutes help to reinforce the competitive strength of the economy in their local region, and throughout Germany and Europe. They do so by promoting innovation, strengthening the technological base, improving the acceptance of new technologies, and helping to train the urgently needed future generation of scientists and engineers.

As an employer, the Fraunhofer-Gesellschaft offers its staff the opportunity to develop the professional and personal skills that will allow them to take up positions of responsibility within their institute, at universities, in industry and in society. Students who choose to work on projects at the Fraunhofer Institutes have excellent prospects of starting and developing a career in industry by virtue of the practical training and experience they have acquired.

The Fraunhofer-Gesellschaft is a recognized non-profit organization that takes its name from Joseph von Fraunhofer (1787–1826), the illustrious Munich researcher, inventor and entrepreneur.

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FRAUNHOFER-INTERNAL NETWORKING

Successful research requires scientific exchange – one of the reasons why Fraunhofer ITEM is well networked within the Fraunhofer-Gesellschaft. Fraunhofer Institutes working in related subject areas cooperate in Fraunhofer Groups and Alliances dedicated to specific topics to coordinate the development of appropriate solutions along the entire value chain. In addition, Fraunhofer Institutes cooperate in Fraunhofer research programs. In pre-competitive research projects, they work out a solid basis for contract research geared to practical applications.

Fraunhofer Group for Life Sciences

Six Fraunhofer Institutes and a Fraunhofer Research Institution, each having proven in-depth expertise in different areas within the life sciences, are involved in the Fraunhofer Group for Life Sciences: the Fraunhofer Institutes IBMT, IGB, IME, ITEM, IVV, and IZI, and the Fraunhofer Research Institution EMB. Their combined knowledge of biology, chemistry, biochemistry, biotechnology, medicine, pharmacology, ecology, and nutritional science is pooled and synergized within this Fraunhofer Group – to allow solutions to be provided even for clients with complex requirements.

Fraunhofer Nanotechnology Alliance

The Fraunhofer Nanotechnology Alliance covers the whole R&D value chain from applied research to industrial implementation. The focus is on nanomaterials, nanobiotechnology, nano-processing and handling, nano-optics and electronics, measuring methods and techniques, and technology transfer and consulting. Fraunhofer ITEM is bringing in its expertise in the fields of toxicology and safe handling of nanoparticles.

Research project RIBOLUTION

In the project RIBOLUTION, five Fraunhofer Institutes are taking an innovative approach to identifying new biomarkers for modern diagnostic solutions. Their aim is to identify novel biomarkers based on ribonucleic acids that can serve as diagnostic indicators or enable prediction of disease progression or future therapy response, and develop these to the point of clinical proof of concept. In this project, Fraunhofer ITEM is screening for COPD biomarkers.

Research project TheraVision

The aim of the Fraunhofer project TheraVision is to develop a platform technology for the development, manufacturing and testing of anticancer viruses. The Fraunhofer Institutes IGB, IZI, ITWM, IME, and ITEM want to jointly develop an oncolytic virus enabling targeted treatment of non-small-cell lung carcinoma (please refer to page 28 for more information).

Research project MyCellFight

For this ambitious research project, the Fraunhofer Institutes IGB, IMW, IZI, IOSB, IPA, and ITEM have teamed up. The aim is to develop an automated immune chip enabling prediction of the specific immunological responses to a drug or chemical of up to 100 individuals at the same time.

Research project SynergyBoost

The Fraunhofer project SynergyBoost is aimed at making a significant contribution to the development of strategies for the fight against implant-associated infections. In this project, the collaborating Fraunhofer Institutes IME, IZI, IFAM and ITEM are investigating synergistic combinations of active agents.

Fraunhofer Cluster of Excellence ImmuVision

In the Fraunhofer Cluster of Excellence dedicated to immune-mediated diseases, the Fraunhofer Institutes IZI, IME, and ITEM constitute a virtual institute where they pool their expertise to develop personalized medicines and therapies for disorders caused by malfunction of the immune system.

NAMES, DATES, EVENTS

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Theses

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Tan Tan
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[Design and construction of a work function measuring station for free electron emitters.]
Leibniz University Hannover, 2017

Granitzny, Anne
In vitro/ex vivo liver models for the prediction of idiosyncratic drug-induced liver injury.
University of Veterinary Medicine Hannover, 2017

Hosseini, Hedayatollah
Molecular mechanism of early breast cancer dissemination.
University of Regensburg, 2017

Requardt, Hendrik
Polyethylene gycol-funtionalized multi-walled carbon nanotubes for nano-material application as drug carriers.
University of Veterinary Medicine Hannover, 2017

Diploma theses

Kirchhoff, David
Entwicklung eines Prüfsystems zur beschleunigten, druckbelasteten Lebens-dauertestung von aktiven polymeren Implantatprüfkörpern.
Leibniz University Hannover, 2017

Master's theses

Baving, Marvin
Characterization of lung basal stem and progenitor cells in teratomas generated by human induced pluripotent stem cells.
Hannover Medical School, 2017

Bettinger, Adenike
Eintrag von Bioziden über Krankenhausabwässer in Kläranlagen.
University of Applied Sciences Emden/Leer, 2017

Carstensen, Saskia
Establishment of a workflow for analytics of novel clinical biomarkers exemplified by the facilitated allergen binding assay in clinical allergen immunotherapy trials.
Hannover Medical School, 2017

Dragon, Anna
Characterisation of the tumour microenvironment of disseminated melanoma cells in human lymph node tissue and cells of peripheral blood ex vivo.
Hannover Medical School, 2017

Hannawald, Melanie
Analyse zirkulierender Tumorzellen von Brustkrebspatientinnen.
University of Regensburg, 2017

Jakimovski, Filip
Entwicklung und Charakterisierung eines additiven Fertigungsprozesses für den 3D-Druck von polymeren Leitermaterialien in der Neuroimplantatfertigung.
Leibniz University Hannover, 2017

Kossow, Wiebke Elisabeth
Aspekte des Vulkanisationsverhaltens von Silikonkautschuken für die Anwendung in der Medizintechnik.
Leibniz University Hannover, 2017

Krämer, Nadine
Pseudomonas aeruginosa induziert eine angeborene Immunantwort in frischem Lungengewebe ex vivo.
Hannover Medical School, 2017

Maatsch, Hannah
Influence of cryopreservation on immune cells in fresh lung tissue.
Hannover Medical School, 2017

Moer, Jana
Isolation, Charakterisierung und Kryokonservierung von naïven T-Zellen aus humanen Lymphknoten.
Charité – Universitätsmedizin Berlin, 2017

Mönkediek, Florian
Thermodynamische Optimierung eines Befeuchters zur inhalativen Gabe von Surfactant bei Frühgeborenen.
[Thermodynamical optimization of a humidifier for the inhalation of surfactant for premature infants.]
Jade University of Applied Sciences Wilhelmshaven, 2017

Schwieters, Magnus
Untersuchung der Tropfenausbreitung von flüssigen Polydimethylsiloxanen auf verschiedenen Substratmaterialien in einem 3D-Druckverfahren für Neuro-implantate.
Leibniz University Hannover, 2017

Sebastian, Ramona
Analyse des Rekrutierungsverfahrens von Studienteilnehmern in der Abteilung "Klinische Atemwegsforschung" am Fraunhofer-Institut für Toxikologie und Experimentelle Medizin ITEM – Strategien zur Verbesserung.
Beuth University of Applied Sciences Berlin, 2017

Bachelor's theses

Behrens, Ailke
Entwicklung eines Verfahrens zur Anwendung von Carbon Nanotube-Silikon-kautschuk auf neuronalen Elektroden.
Jade University of Applied Sciences Wilhelmshaven, 2017

Börgmann, Hazel
Entwicklung und Integration einer Mehrkomponentenplattform in einen 3D-Druckprozess von Neuroimplantaten.
Jade University of Applied Sciences Wilhelmshaven, 2017

Greinert, Daniel
Effekte von immunmodulierenden Substanzen auf die Funktion von Leukozyten.
University of Applied Sciences Emden/Leer, 2017

Hadeler, Steffen
Entwicklung eines Fertigungsverfahrens für selbstkrümmende Cochlea-Implantate.
Leibniz University Hannover, 2017

Heidenreich, Jan-Christian
Gene expression profiling of disseminated prostate cancer cells.
University of Regensburg, 2017

Labisch, Julia
Langzeitkultivierung von Lungenfrischgewebe im perfundierten Biochip.
Bielefeld University, 2017

Lührs, Janita
Untersuchung der anti-infektiven Aktivität von Makrophagen in einem Ex-vivo-Ko-Kultursystem mit Precision-Cut Lung Slices (PCLS).
Georg-August-Universität Göttingen, 2017

Moser, Lena Maria
Analyse zirkulierender Tumorzellen auf aktivierende Mutationen im ESR1-Gen bei Östrogenrezeptor-positiven Brustkrebspatientinnen mit fortgeschrittenem Mammakarzinom.
University of Regensburg, 2017

Muehlbauer, Franziska-Anna
Development of allele-specific PCR assays for detection of hot-spot mutations in whole genome amplification products.
University of Regensburg, 2017

Selle, Michael
Auswertung toxikologischer Daten mithilfe der Hauptkomponentenanalyse – Klassifizierung nach Toxizität.
University of Applied Sciences Emden/Leer, 2017

Wöhrl, Lukas
Introduction of a *TP53* EXON-6 truncating mutation into breast cell lines.
University of Regensburg, 2017

Invited lectures

Dr. Philipp Badorrek
A missing link in study plan implementation?
PCMG Annual Conference 2017
Copenhagen (Denmark), June 9, 2017

Recruitment from the perspective of an investigative site – pitfalls and strategies.
Partnership in Clinical Trials (PCT) Congress 2017
Amsterdam (The Netherlands), November 28, 2017

Prof. Dr. Armin Braun
Neues aus der Zellbiologie des Hustens – das Immunsystem.
58th Annual Congress of the German Respiratory Society (DGP)
Stuttgart (Germany), March 22-25, 2017

Mechanisms of mast cell-nerve interactions in the lung?
KU Leuven
Leuven (Belgium), August 30, 2017

Use of human ex-vivo precision-cut lung slice infection models to investigate immunological mechanisms and to test anti-infective drugs.
Glycomics Week, Griffith University
Gold Coast (Australia), October 11, 2017

Prof. Dr. Theodor Doll
The future of hearing.
IVAM Congress "Health Business Connect 2017"
Dortmund (Germany), July 5-6, 2017

Atmospheric electrons in nano-based everyday life macroapplications.
Humboldt Kolleg, Nanoscale Science and Technology 2017
Hammamet (Tunisia), October 27-29, 2017

Dr. Sevim Duvar
Current strategies in mammalian cell line development.
Workshop "Therapeutic mAb Engineering and Production"
Izmir (Turkey), November 11, 2017

Dr. Sylvia E. Escher
EU-ToxRisk case studies: NAMs in read-across.
ecopa (European Consensus Platform for Alternatives) SSCT (Scandinavian Society for Cell Toxicology) Workshop
Helsinki (Finland), June 14, 2017

Project B18: Update of the CPDB database and point of departure analysis.
CEFIC-LRI Annual Meeting
Brussels (Belgium), November 16, 2017

EU-ToxRisk: Development of integrated approaches to testing and assessment (IATA) – Introduction to case study concept.
Meeting of the PARERE network at the European Commission's Joint Research Center (JRC)
Ispra (Italy), November 28, 2017

Read-across case studies on (un)branched carboxylic acids which induce micro-vesicular liver steatosis.
Meeting of the PARERE network at the European Commission's Joint Research Center (JRC)
Ispra (Italy), November 28, 2017

Dr. Stefan Hahn
Praktische Erfahrungen mit den Datenanforderungen für das Produktdossier.
Fresenius conference "Biozide: Bewertung und Zulassung"
Cologne (Germany), October 17, 2017

Dr. Christina Hesse
Description of pro-fibrotic biomarkers in precision-cut lung slices (PCLS).
Annual Meeting 2017 of the Japanese Respiratory Society
Tokyo (Japan), April 22, 2017

Prof. Dr. Jens Hohlfeld
Quantification of airway inflammation following endobronchial allergen and endotoxin challenge with magnetic resonance imaging.
2017 International Workshop on Pulmonary Imaging
Philadelphia, Pennsylvania (USA), March 2-4, 2017

Asthma – U-BIOPRED.
58th Annual Congress of the German Respiratory Society (DGP)
Stuttgart (Germany), March 22-25, 2017

Dr. Olaf Holz
Early experiences in LPS study.
PExA (particles in exhaled air) 2017 event
Milan (Italy), September 10, 2017

Prof. Dr. Christoph Klein
Early dissemination and metastasis formation: do we need novel therapeutic concepts?
BBC Special Lecture
Basel (Switzerland), January 24, 2017

Frühe Streuung und ektope Progression von Krebszellen: Konsequenzen für die Diagnostik und Therapie.
8. Akademie "Knochen und Krebs"
Munich (Germany), May 5-6, 2017

Early cancer cell dissemination with and without parallel progression.
2017 International Conference "Cancer of Unknown Primary" (CUP)
Torino (Italy), May 20-21, 2017

Foundations for precision medicine.
First ISC Workshop on Precision Medicine
Frankfurt/Main (Germany), June 22, 2017

Molekulares Staging – die Zukunft?
101st Annual Conference of the German Society for Pathology
Erlangen (Germany), June 22-24, 2017

Early dissemination and parallel progression in cancer.
3rd International Cancer Symposium of the Cancer Research Center of Lyon (CRCL)
Lyon (France), September 25-27, 2017

Mechanisms of early dissemination and metastasis formation.
Symposium "Dynamics of adult stem cells and cancer"
Frankfurt/Main (Germany), October 25-26, 2017

Early dissemination and evolutionary development of metastasis outside the primary tumor.
1st Brigitte and Dr. Konstanze Wegener Seminar/DCC-Net-Retreat Düsseldorf (Germany), November 3, 2017

Early cancer cell dissemination and metastasis formation.
3rd AEK Autumn School 2017
Berlin (Germany), November 6-8, 2017

Prof. Dr. Wolfgang Koch
Generation and characterization of CNTs in long-term inhalation studies.
AIT Annual Conference 2017
Copenhagen (Denmark), October 26-27, 2017

Prof. Dr. Norbert Krug
Implementierung von Strukturen für frühe klinische Studien. Indikations-übergreifende Modelle: Clinical Research Center Hannover.
Health Research Forum working group on infrastructures in the life sciences
Berlin (Germany), June 14, 2017

Rhinovirus challenge in humans – a model in drug development.
10th International VPM Days
Hannover (Germany), September 15, 2017

Kooperationen im Bereich GXP und klinischer Studien am Beispiel ITEM/MHH.
2nd joint meeting of Deutsche Hochschulmedizin and the Fraunhofer-Gesellschaft
Berlin (Germany), November 1, 2017

Biomarker bei Lungenerkrankungen.
Symposium "Biomarker: Objektive Parameter als Grundlage für die erfolgreiche individuelle Therapie"
Berlin (Germany), November 21, 2017

Dr. Gerhard Pohlmann
Innovative Ansätze zur Therapie mit Aerosolen.
15th Lower Saxony Life Science Day
Braunschweig (Germany), September 11, 2017

Bernhard Polzer
Application of single-cell technologies in clinical samples.
2nd World Precision Medicine Congress
London (UK), May 17-19, 2017

Clinical applications of single-cell analysis.
CELLSEARCH® + DEPArray™ User Meeting
MAST – Bologna (Italy), September 26-27, 2017

Translationales Forschungsnetzwerk DETECT CTC.
9th scientific symposium of AGO-TraFo
Düsseldorf (Germany), October 12-13, 2017

Prof. Dr. Antje Prasse
Zukünftige neue Therapien der IPF.
AIR Meeting
Hamburg (Germany), February 11, 2017

IgG4-assoziierte Lungenerkrankungen.
58nd Annual Congress of the German Respiratory Society (DGP)
Stuttgart (Germany), March 22, 2017

Gender und Lungenfibrose.
58nd Annual Congress of the German Respiratory Society (DGP)
Stuttgart (Germany), March 23, 2017

Pathogenese der IPF.
58nd Annual Congress of the German Respiratory Society (DGP)
Stuttgart (Germany), March 23, 2017

Therapie der Lungenfibrose.
HRCT Thorax Workshop
Hannover (Germany), March 25, 2017

ATS Update ILD.
ATS Update, Aachen University Hospital
Aachen (Germany), June 14, 2017

Update Lungenfibrose.
Lung Clinic Immenhausen
Kassel (Germany), September 2, 2017

Pathogenesis of idiopathic pulmonary fibrosis.
University of Siena
Siena (Italy), September 14, 2017

Update IPF.
University of Florence
Florence (Italy), September 15, 2017

Update IPF.
IPF Expert Meeting at the CRC Hannover
Hannover (Germany), September 20, 2017

Rheuma und Lunge.
Rheumatology/pneumology expert forum at the Hannover Medical School
Hannover (Germany), October 25, 2017

Antifibrotic treatment of IPF.
EU COST Meeting
Prague (Czech Republic), November 3, 2017

Individualisierte Therapie bei ILD.
Professional training course at the Hannover Medical School
Hannover (Germany), December 13, 2017

Dirk Schaudien Ph.D.
The reason you don´t want to inhale carbon nanotubes.
Series of lectures at the Leibniz Institute for Solid State and Materials Research
Dresden (Germany), November 30, 2017

Dr. Franziska Schramm
How to handle critical substances in a biocidal product.
3rd Conference of Applied Hygiene, Microbiology and Virology; Dr. Brill Academy
Hamburg (Germany), November 2-3, 2017

Dr. Sven Schuchardt
Ergebnisse EASA CAQ-Projekt.
BDL Cabin Air Quality Workshop
Frankfurt/Main (Germany), June 26, 2017

Untersuchungen und Ergebnisse über Kabinenluftmessungen im Auftrag der EASA.
Cabin Air Quality Forum of the Lufthansa Group
Frankfurt/Main (Germany), November 21, 2017

Dr. Katherina Sewald
Frischgewebe als Ansatzpunkt für Grundlagenforschung, Toxikologie und Wirksamkeitstestung.
Colloquium at the Bundeswehr Institute for Toxicology
Munich (Germany), July 5, 2017

Ex-vivo lung models as a tool to study respiratory injury and inflammation.
EUROTOX 2017
Bratislava (Slovakia), September 11, 2017

Dr. Christian Werno
Molekulare Charakterisierung disseminierter und zirkulierender Tumorzellen – Chancen für Forschung, Diagnostik und Therapie.
Scientific training course at the university hospital
Frankfurt/Main (Germany), June 20, 2017

Dr. Christina Ziemann
In-vitro-Toxizitätsuntersuchungen zu Varianten der Graphenfamilie.
Meeting of the Fraunhofer Nanotechnology Alliance
Hannover (Germany), April 5, 2017

PLATOX – In-vitro- und In-vivo-Untersuchungen zur Generierung validierter Toxizitätsdaten für Graphen-Nanoplättchen.
NanoCare Cluster Meeting 2017
Karlsruhe (Germany), May 5, 2017

Ariane Zwintscher
Data requirements, authority updates and several pitfalls in BPR.
3rd Conference of Applied Hygiene, Microbiology and Virology; Dr. Brill Academy
Hamburg (Germany), November 2-3, 2017

Biozide – Grundlagen und aktuelle Herausforderungen – Tutorium/Beschichtungen und Bauchemie.
Farbe und Lack Conference
Kassel (Germany), November 14, 2017

Contributions to congresses and conferences

Behrens, A.; Tegtmeier, K.; Doll, T.
Evaluation of applicability of carbon nanotube-silicone rubber on electrode arrays.
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Boge, L.; Müller, M.; Jonigk, D.; Braubach, P.; Fieguth, H. G.; Warnecke, G.; Krüger, M.; Braun, A.; Sewald, K.; Wronski, S.
Infection of fresh human lung tissue with *P. aeruginosa*.
DZL Fall Conference
Gießen (Germany), November 10-11, 2017

Brueggemann, M.; Licht, O.; Fetter, E.; Teigeler, M.; Schaefers, C.; Eilebrecht, E.
The endocrine axes of fish and amphibians share common key events identified using the concept of Adverse Outcome Pathways (AOP).
SETAC Europe 27th Annual Meeting
Brussels (Belgium), May 7-11, 2017

Erffmeier, L.; Curths, C.; Dahlmann, F.; Knauf, S.; Kaup, F.-J.; Braun, A.; Sewald, K.; Bleyer, M.
Morphometric analyses in the conducting airways of house dust mite-challenged common marmosets (*Callithrix jacchus*).
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Escher, S.
Prediction of systemic toxicity after repeated exposure by new approach methodologies (NAMs) – is a prediction of STOR-RE classification possible?
19th Annual Cefic-LRI Workshop
Brussels (Belgium), November 16, 2017

Escher, S.; Kellner, R.
Update of the carcinogenic potency database + analysis of thresholds of toxicological concern.
OPENTOX Europe
Basel (Switzerland), November 21-23, 2017

Gabbert, S.; Hahn, S.; Klein, M.; Nendza, M.; Oosterhuis, F.
A benchmark-level approach for evaluating PBT and vPvB chemicals in REACH.
SETAC Europe 27th Annual Meeting
Brussels (Belgium), May 7-11, 2017

Hahn, T.; Floeter, C.; Schwonbeck, S.; Könnecker, G.
When is a substance a "natural substance"? A case study in the context of the EU veterinary medicines market authorization procedure.
ICCE – 16th international conference on Chemistry and the Environment
Oslo (Norway), June 18-22, 2017

Hassel, A. W.; Kollender, J. P.; Sprinzl, G.; Doll, T.
Corrosion of active implant materials for cochlear hearing aids and cardiac pacemakers.
EUROCORR 2017 & 20th ICC – International Corrosion Council
Prague (Czech Republic), September 3-7, 2017

Hesse, C.
Description of pro-fibrotic Biomarkers in precision-cut lung slices (PCLS).
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Hohlfeld, J.
Safety and efficacy of human rhinovirus-16 (U-BIOPRED) in healthy volunteers and patients with asthma on inhaled steroids.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Hohlfeld, J.
Lung deflation with indacaterol/glycopyrronium improves cardiac function in COPD patients: the CLAIM study.
ERS (European Respiratory Society) International Congress 2017
Milan (Italy), September 11, 2017

Holz, O.; Gaida, A.; Lavae-Mokhtari, B.; Kruse, L.; Schuchardt, S.; Hohlfeld, J. M.
Breath volatile organic compounds (VOC) in COPD – first results from a large validation trial.
6th Annual Meeting of the German Center for Lung Research (DZL)
Munich (Germany), January 30-31, 2017

Jäger, B.; Wirtz, V.; Carleo, A.; Terwolbeck, O.; Prasse, A.
3D organoid model for in-vitro testing of medical compounds.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Jakimovski, F.; Stieghorst, J.; Doll, T.
Irradiation induced heating of silicone rubber on different substrates.
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Jiménez Delgado, S. M.
Mast cell nerve interaction in the lung.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Konzok, S.; Dehmel, S.; Braubach, P.; Krüger, M.; Jonigk, D.; Pfennig, O.; Fieguth, H. G.; Braun, A.; Sewald, K.
Bevacizumab and cisplatin show anti-cancer effects in a dynamic cancer cell-invaded ex-vivo lung tissue system.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Küppers, L.; Holz, O.; Lavae-Mokhtari, B.; Günther, F.; Häsler, L.; Zang-Pappa, K.; Gottlieb, J.; Hohlfeld, J. M.
Breath VOC patterns of lung transplant recipients with and without chronic lung allograft dysfunction (CLAD).
6th Annual Meeting of the German Center for Lung Research (DZL)
Munich (Germany), January 30-31, 2017

Mang, S.; Braun, A.; Lamb, D.
COPD patient isolated *H. influenzae* stimulates M1 macrophages to produce interleukins 1α/β which synergistically drive transepithelial signaling.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Marcoleta, J. P.; Froriep, U.; Nogueira, W.; Lenarz, T.; Doll, T.
Distributed multiplexing system for ECoG.
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Obernolte, H.; Ritter, D.; Knebel, J.; Braubach, P.; Jonigk, D.; Warnecke, G.; Krüger, M.; Fieguth, H. G.; Pfennig, O.; Braun, A.; Sewald, K.
Cigarette smoke induced inflammation and cytotoxicity in viable lung tissue.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Pankalla, J.; Doll, T.; Pohlmann, G.
Testing bench for accelerated life cycle testing (ALCT).
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Prasse, A.
Recapitulation of embryogenesis: bronchosphere generation as a disease model for drug testing.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Schwieters, M.; Stieghorst, J.; Doll, T.
Droplet spreading of polydimethylsiloxanes on different substrate materials for the 3D printing of neural implants.
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Schwonbeck, S.; Hahn, T.; Könnecker, G.
The paradox of legacy products – what do we do with new information on fate and environmental effects of legacy pharmaceuticals in generic veterinary medicines?
SETAC Europe 27th Annual Meeting
Brussels (Belgium), May 7-11, 2017

Tan, T.; Marcoleta, J. P.; Hassel, A. W.; Doll, T.
Absolute value work function measurement for ambient atmosphere photo-emissive thin films.
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Wackers, G.; Cornelis, P.; Givanoudi, S.; Khorshid, M.; Ramakers, G.; Tack, J.; Doll, T.; Trost, F.; Junkers, T.; Wagner, P.
Towards a catheter-based sensor for the electronic detection of histamine in the intestinal tract.
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Walter, D.; Schaudien, D.; Sewald, K.; Braun, A.; Hoymann, H.-G.
Bleomycin-induced pulmonary fibrosis in rats and mice shows similar progression in lung function, biochemical and histological analyses.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Werno, C.; Weidele, K.; Treitschke, S.; Botteron, C.; Scheitler, S.; Haferkamp, S.; Polzer, B.; Werner-Klein, M.; Klein, C. A.
Preclinical in vitro/in vivo models from disseminated tumor cells.
2nd Annual World Preclinical Congress Europe
Lisbon (Portugal), November 15-17, 2017

Wiegandt, F.
Pre-triggered dry and liquid aerosol release inside the patient interface of preterm neonates.
21st Congress of the International Society of Aerosols in Medicine (ISAM)
Santa Fe, New Mexico (USA), June 3-7, 2017

Wiegandt, F.
Stretchable microfabricated strain sensor array foil for the usage of triggered drug delivery for preterm neonates.
EnFI 2017 – Engineering of Functional Interfaces
Marburg (Germany), August 28-29, 2017

Wiegandt, F.
Breath-activated drug delivery for preterm neonates and adults using a continuous powder aerosolizer.
Inhaled Therapies for Tuberculosis and other Infectious Diseases, 4th International TB-Meeting
Durham, North Carolina (USA), October 16-17, 2017

Wirtz, V.; Jäger, B.; Engelhard, P.; Prasse, A.
A new humanized mouse model of idiopathic pulmonary fibrosis (IPF).
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Zmora, P.; Blazejewska, P.; Bertram, S.; Walendy-Gnirß, K.; Nehlmeier, I.; Lins, A.; Moldenhauer, A. S.; Konzok, S.; Dehmel, S.; Sewald, K.; Brinkmann, C.; Curths, C.; Knauf, S.; Gruber, J.; Mätz-Rensing, K.; Dahlmann, F.; Braun, A.; Pöhlmann, S.
Cleavage and activation of the influenza virus hemagglutinin by non-human primate orthologues of TMPRSS2.
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 19-20, 2017

Active participation in committees

Dr. Annette Bitsch
German Federal Institute for Risk Assessment (BfR) Committee for Food Additives, Flavorings and Processing Aids

Working committee on probabilistic exposure and risk assessment "Probabilistische Expositions- und Risikoabschätzung"

Expert panel 110 on cooling lubricants "Kühlschmierstoffe" of the Association of German Engineers (VDI) Technical Division 1 "Production Technology and Manufacturing Methods"

Reviewer for international journals published by Elsevier (incl. "Regulatory Toxicology and Pharmacology")

Katharina Blümlein Ph.D.
Working group on analyses in biological materials "Analysen in biologischem Material" of the German Research Foundation (DFG)

Prof. Dr. Armin Braun
External assessor for international foundations

MD/Ph.D. commission "Molecular Medicine" of the Hannover Medical School

Scientific advisory committee of the German Society for Allergology and Clinical Immunology (DGAKI)

Member of the German Center for Lung Research (DZL)

Reviewer for international journals in respiratory medicine and immunology (incl. "Journal of Allergy and Clinical Immunology")

Dr. Otto Creutzenberg
Reviewer for international journals in particle and fiber toxicology ("Particle and Fibre Toxicology", "Inhalation Toxicology")

Prof. Dr. Clemens Dasenbrock
Scientific Council on Electromagnetic Fields of the Swedish Radiation Safety Authority (SSM)

Prof. Dr. Theodor Doll
VDE/VDI Society Microelectronics, Microsystems and Precision Engineering GMM, chair of the expert panel on microsystems in medicine/functional surfaces "FA 4.6 Mikrosysteme in der Medizin/Funktionale Oberflächen"

German Society for Biomedical Engineering DGBMT, expert panel on sensor technology "Sensorik"

Reviewer in the European Commission's Marie Skłodowska-Curie Actions (MSCA) program, expert in the work packages "Biomedical Technologies" and "Sensors" of the EU Graphene Flagship

ASIIN reviewer for biomedical engineering careers

Guest editor of the journal "Physica Status Solidi (a)"

Uta Dörfel
Working groups on GLP analytics "GLP-Analytik" and medical devices "Medizinprodukte" of the German Quality Management Association (GQMA; former German Society for Good Research Practice (DGGF))

Dr. Heinrich Ernst
"Guess What" committee of the European Society of Toxicologic Pathology (ESTP)

INHAND (International Harmonization of Nomenclature and Diagnostic Criteria) organ working groups "Soft Tissue" and "Skeletal System"

Editorial board of the journal "Experimental and Toxicologic Pathology"

Reviewer for the international journal "Toxicologic Pathology"

Dr. Sylvia Escher
Threshold of Toxicological Concern Task Force, ILSI Europe (co-chair)

Dr. Ilona Fleischhauer
Working groups on GLP quality assurance/monitoring "GLP: Qualitätssicherung/Überwachung" and GCP quality management "GCP-Qualitätsmanagement" of the German Quality Management Association (GQMA; former German Society for Good Research Practice (DGGF))

Head of the working committee on quality management "Qualitätsmanagement im VLS" in the Fraunhofer Group for Life Sciences

Dr. Stefan Hahn
Working committee on chemical risk assessment of the German Chemical Society (GDCh) division of environmental chemistry and ecotoxicology "Umweltchemie und Ökotoxikologie"

Dr. Roman Halter
External expert in the quality control committee of the association for mineral wool quality "Gütegemeinschaft Mineralwolle e. V."

Martina Heina
IT division of the International Association for Pharmaceutical Technology (APV)

Prof. Dr. Dr. Uwe Heinrich
Invited member of the IARC working groups on particles, fibers, diesel engine exhaust, polycyclic aromatic hydrocarbons, metals, irritant gases, and air pollution for the compilation of IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

DFG Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission): working group on the definition of threshold limit values for dusts; working group on the definition of occupational exposure limits; working group on the classification of carcinogens; ad-hoc working group on heavy metals

Committee on Hazardous Substances (AGS) under the German Federal Minister of Labor and Social Affairs; AGS Subcommittee III (UA III); Subcommittee III: working groups on metals (chairman) and on fibers/dust

Advisory committee of the Institute for Prevention and Occupational Medicine (IPA) of the German Social Accident Insurance (DGUV)

Committee supporting the public authorities responsible for the approval of animal experiments (Animal Protection Commission)

Co-editor of the manual on hazard assessment of environmental pollutants "Gefährdungsabschätzung von Umweltschadstoffen"

Prof. Dr. Jens Hohlfeld
External assessor for the German Research Foundation (DFG)

Steering committee of the research network "Biomedical Research in Endstage And ObsTructive Lung Disease Hannover" (BREATH) within the German Center for Lung Research (DZL)

Scientific advisory group of the European Medicines Agency (EMA)

Reviewer for international journals (incl. "American Journal of Respiratory and Critical Care Medicine", "European Respiratory Journal", and "Journal of Allergy and Clinical Immunology")

Dr. Olaf Holz
IABR (International Association of Breath Research) Standardization Focus Group

Reviewer for international journals (incl. "European Respiratory Journal", "PLOS ONE", "Respiratory Research", and "BMC Pulmonary Medicine")

Dr. Kamran Honarnejad
Reviewer for the international journal "SLAS Discovery" (previous title: "Journal of Biomolecular Screening")

Michéla Kaisler
Working group on archiving "Archivierung" of the German Quality Management Association (GQMA; former German Society for Good Research Practice (DGGF))

Dr. Rupert Kellner
Councilor for electronic communication and member of the Executive Board of the European Society of Toxicologic Pathology (ESTP)

Global Editorial and Steering Committee (GESC) for the initiative "International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice" (INHAND)

Prof. Dr. Christoph Klein
External assessor for "Lichtenberg Professorships" of the Volkswagen Foundation

External assessor for numerous national and international organizations and foundations: German Research Foundation, German Federal Ministry of Education and Research, Wilhelm Sander Foundation for Cancer Research, ERC, Deutsche Krebshilfe, Dutch Cancer Society, Association for International Cancer Research, EU-FP7, MRC, Cancer Research UK, Kegg-Foundation

Deputy chairman of the scientific committee of Comprehensive Cancer Center Ostbayern (CCCO)

Reviewer for international journals in oncology (incl. "Nature", "Nature Biotechnology", "Nature Cell Biology", "Nature Medicine", "Cancer Cell", "Science", "PNAS", "American Journal of Pathology", "Cancer Research", "Clinical Cancer Research", "International Journal of Cancer", "Nucleic Acid Research", »European Journal of Immunology", "Lancet Oncology", "European Journal of Cancer", "PLOS ONE", and "Oncotarget")

Prof. Dr. Wolfgang Koch
Reviewer for international journals in aerosol physics and aerosol technology (incl. "Journal of Aerosol Science", "Aerosol Science and Technology" and "Annals of Occupational Hygiene")

Dr. Gustav Könnecker
Working group on European chemicals policy "Europäische Chemikalienpolitik" of the 6th governmental commission "Energie- und Ressourceneffizienz" of the Land Lower Saxony.

Integrated REACH project team, German Federal Office of Bundeswehr Equipment, Information Technology and In-Service Support

Prof. Dr. Norbert Krug
Scientific advisory committee of the German Society for Allergology and Clinical Immunology (DGAKI)

Board member of the interdisciplinary allergy center of the Hannover Medical School

Chair of the Clinical Trial Board of the German Center for Lung Research (DZL)

Steering committee of the research network "Biomedical Research in Endstage And ObsTructive Lung Disease Hannover" (BREATH) within the German Center for Lung Research (DZL)

External assessor for the German Research Foundation (DFG)

External assessor for the American Chemistry Council

Advisory board of the expertise network "Asthma und COPD"

Deputy chairman of the Fraunhofer Group for Life Sciences

Reviewer for international journals in allergology, immunology, and respiratory diseases

Dr. Nico Langer
GMP discussion group "GMP-Gesprächskreis" of the Lower Saxony business inspectorate

Dr. Oliver Licht
German Federal Institute for Risk Assessment (BfR) Committee for Contaminants and other Undesirable Substances in the Food Chain; chair of the panel on per- and polyfluorinated alkyl substances "Per- und Polyfluoralkylsubstanzen (PFAS)"

Expert panel "Basic module and perfluorinated tensides" of the German Federal Institute for Risk Assessment's MEAL (= meals for exposure assessment and analysis of foods) study within the Total Diet Study (TDS) in Germany

Working committee on regulatory toxicology "Regulatorische Toxikologie" of the German Society of Toxicology within the German Society of Clinical and Experimental Pharmacology and Toxicology (DGPT)

Public relations delegate of the German Society of Toxicology

Dr. Norbert Lüthe
Working group on electronic data processing "EDV" of the German Quality Management Association (GQMA; former German Society for Good Research Practice (DGGF))

Fraunhofer quality management network

Dr. Neophytos Papamichael
Working committee on quality management "Qualitätsmanagement im VLS" in the Fraunhofer Group for Life Sciences

GMP discussion group "GMP-Gesprächskreis" of the Lower Saxony business inspectorate

Dr. Gerhard Pohlmann
International Society of Aerosols in Medicine (ISAM)

Dr. Bernhard Polzer
External assessor for the Wilhelm Sander Foundation for Cancer Research

External assessor for the Medical Research Council (UK)

Reviewer for international journals in pathology and oncology ("British Journal of Cancer", "International Journal of Cancer", "Journal of Histochemistry and Cytochemistry", "Oncotarget", and "Thoracic Cancer")

Prof. Dr. Antje Prasse
External assessor for the German Research Foundation (DFG)

Board member of the Scientific Working Group for the Therapy of Lung Diseases (WATL)

Board member of Deutsche Atemwegsliga

Spokesperson for the disease area "DPLD" in the research network "Biomedical Research in Endstage And ObsTructive Lung Disease Hannover" (BREATH) within the German Center for Lung Research (DZL)

Coordinator of the ILD group in the European Reference Network on Respiratory Diseases ERN-LUNG

Deputy spokesperson of the Cell Biology Section in the German Respiratory Society (DGP)

Reviewer for international journals (incl. "American Journal of Respiratory and Critical Care Medicine", "European Respiratory Journal", "American Journal of Respiratory and Cell Biology", and "Thorax")

Associate editor of "PLOS ONE"

Priv.-Doz. Dr. Susanne Rittinghausen
Co-optive member of the European Society of Toxicologic Pathology (ESTP) board: representative for nomenclature

"Guess What" committee of the European Society of Toxicologic Pathology (ESTP)

Global Editorial and Steering Committee (GESC) for the initiative "International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice" (INHAND)

INHAND (International Harmonization of Nomenclature and Diagnostic Criteria) organ working groups "Respiratory System", "Endocrine System", "Soft Tissue", and "Special Senses", and working group "Apoptosis"

Associate editor of the international journal "Toxicologic Pathology"

Editorial board of the journal "Experimental and Toxicologic Pathology"

Dirk Schaudien Ph.D.
INHAND (International Harmonization of Nomenclature and Diagnostic Criteria) working group "Non-rodents: minipig"

"Pathology 2.0" committee of the European Society of Toxicologic Pathology (ESTP)

Dr. Sven Schuchardt
Working group on air analyses "Luftanalysen" of the German Research Foundation (DFG)

GBM – Society for Biochemistry and Molecular Biology

Leibniz-Institut für Analytische Wissenschaften – ISAS – e. V. (Leibniz Institute for Analytical Sciences)

Scientific committee for the EU project FACTS (investigations to find FACTS on the subject of aircraft cabin air quality)

Reviewer for international journals in biochemistry and analytics (incl. "Journal of Proteome Research", "Proteomics", "Electrophoresis", and "Talanta")

Dr. Katherina Sewald
External assessor for international research grants

Steering group of the workshop "Respiratory Toxicity"

Steering group of the workshop "Translational Aspects of in vitro and in vivo Models for Inflammatory Diseases"

Reviewer for the international journals "Toxicology Letters", "Toxicology in Vitro", "Nanotoxicology", "ATOX", and "PLOS ONE"

Dr. Holger Ziehr
Association of German Engineers (VDI) committee "Technical Good Manufacturing Practice"

GMP discussion group "GMP-Gesprächskreis" of the Lower Saxony business inspectorate

Center for Pharmaceutical Process Engineering (PVZ) at Technische Universität Braunschweig

BioPharma-Translationsinstitut e. V.

Dr. Christina Ziemann
Working group "Genotoxicity" of the DIN Water Practice Standards Committee

Working group on threshold mechanisms of genotoxins of the Geman Society for Environmental Mutation Research (GUM)

Working group on statistics of the Geman Society for Environmental Mutation Research (GUM)

Working group on carcinogenesis "Carcinogenese" of the German Society of Toxicology

Teaching activities

Prof. Dr. Armin Braun
TRAIN Academy: professional education program "Translational Research & Medicine: From Idea to Product" (lecturer and person in charge of Module 6 "Preclinical development")

Hannover Medical School: lectures in the MD/Ph.D. program "Molecular Medicine"

7th Lower Saxony International Summer Academy in Immunology at the Hannover Medical School: lecture on "Neuroimmune interactions in allergic asthma" in the session "Lung Inflammation, Asthma, Allergy"

Dr. Zbigniew Czyz
University of Regensburg: course in pathology in the degree course "Molecular Medicine"

Prof. Dr. Clemens Dasenbrock
University of Veterinary Medicine Hannover, Foundation: Toxicologic Pathology Training Program, Module 4 "Respiratory tract": Introduction to (animal experimental) inhalation toxicology

TRAIN Academy, Module 6 "Preclinical development": Toxicological testing of small molecules and biologicals

Prof. Dr. Theodor Doll
Leibniz University Hannover: lecture on microplastics for implant production in the degree course "Biomedical Engineering"

Hannover Medical School: postgraduate training course in nanomedicine

Jade University of Applied Sciences in Wilhelmshaven: lecture on biomechanics, breathing and neuro-rehabilitation in the degree course "Medical Technology"

TRAIN Academy: lectures on economic aspects in implant development

Dr. Ilona Fleischhauer
German Primate Center, Göttingen: lecture on introduction to the GLP guidelines within the "Laboratory Animal Science Course on Primates"

TRAIN Academy: lectures on quality management and Good Laboratory Practice (GLP)

Prof. Dr. Jens Hohlfeld
Hannover Medical School: lectures on allergic respiratory diseases

Dr. Stefan Kirsch
University of Regensburg: lectures and hands-on training in molecular oncology in the degree course "Molecular Medicine"

Prof. Dr. Christoph Klein
University of Regensburg: lectures in pathology and molecular oncology in the degree course "Molecular Medicine"; course and hands-on training in molecular oncology; lectures on pathology in the degree course "Human Medicine"

Ostbayerische Technische Hochschule Regensburg: lecture "What is metastatic dissemination?" in the degree course "Medical Information Technology" (part of the series of introductory lectures into the different subject matters of medicine")

Dr. Oliver Licht
RWTH Aachen: lectures in toxicology and risk assessment

Governmental Institute of Public Health of Lower Saxony (NLGA) in Hannover: lecture on substance assessment and risk assessment within the DGPT course "Regulatory Toxicology"

German chemical society (GDCh) training course "Introduction to toxicology for chemists" in Hannover: lecture on REACH/chemical regulation

Dr. Gerhard Pohlmann
Jade University of Applied Sciences in Wilhelmshaven: lecture on biomechanics, breathing and neuro-rehabilitation in the degree course "Medical Technology"

TRAIN Academy: lectures on economic aspects in implant development and in Module 6 "Preclinical Development of Medical Devices"

Dr. Bernhard Polzer
University of Regensburg: lectures on pathology and molecular oncology in the degree course "Molecular Medicine"; hands-on training in molecular oncology

Prof. Dr. Antje Prasse
Hannover Medical School: lectures on interstitial lung disease

Priv.-Doz. Dr. Susanne Rittinghausen
University of Veterinary Medicine Hannover, Foundation: courses in toxicological pathology

Dr. Anton Roß
Hamburg University of Applied Sciences: lectures in Good Manufacturing Practice (GMP)

Dirk Schaudien Ph.D.
University of Veterinary Medicine Hannover, Foundation: lectures and courses in special and toxicological pathology

Dr. Katherina Sewald
Hannover Medical School: lectures on allergy and asthma and on analgesics in the degree course "Biomedicine"; lectures on hypertension in the degree course "Biochemistry"; laboratory course in biomedicine; laboratory course in biochemistry: immunology

REBIRTH Autumn Academy for Teachers: course and hands-on training

TRAIN Academy: lectures on immunotoxicology

Dr. Henning Weigt
TRAIN Academy: lectures on "Principles of quality management – risk management, audits, deviation and change management" and "Preclinical development, phases, costs, and quality assurance"

Dr. Christian Werno
University of Regensburg: lectures on pathology and molecular oncology in the degree course "Molecular Medicine"; hands-on training in molecular oncology

Dr. Holger Ziehr
RWTH Aachen: lectures on "Regulatory Affairs"

Technische Universität Braunschweig lectures on applied and technical biochemistry

Dr. Christina Ziemann
German chemical society (GDCh) training course 157/17 "Introduction to toxicology for chemists" in Hannover: lecture on genetic toxicology

German Academic Scholarship Foundation lecture group on nanotechnology: lecture and lab tour on "Toxicity of nanomaterials"

Publicly funded research projects

National

DFG – German Research Foundation
Experimental exposure to air pollutants and sympathetic nerve activity in human subjects

From Regenerative Biology to Reconstructive Therapy (REBIRTH 2). Excellence cluster

Clinical Research Unit 311: Advanced cardiac and pulmonary failure: mechanical unloading and repair

Identification of tumor-specific peptides for adjuvant immunotherapy of melanoma patients without distant metastasis

DFG priority program "Mast Cells – Promoters of Health and Modulators of Disease" (SPP 1394)
Characterization of mast cell anatomy and function in primate airways – interaction with the nervous system. DFG Br2126/3-1

Federal Environment Agency
Chronic toxicity/carcinogenicity assessment of selected nanomaterials.
R&D project 3712 61 206

Support for the use of computerized calculations such as quantitative structure-activity relationships (QSAR methods) to reduce animal experiments under REACH. R&D project 3714 67 413 0

Animal-free assessment under REACH – further development and application of read-across. R&D project 3715 67 418 0

Relevance of physiological and anthropometric parameters for the standardization and assessment of human biomonitoring results. R&D project 3716 62 214 0

Human biomonitoring of "novel" substances: substance dossier for Lysmeral – derivation of toxicological assessment values for human biomonitoring. Project number 58 759

Human biomonitoring of "novel" substances: substance dossier for 2,6-di-tert-butyl-4-methylphenol – derivation of toxicological assessment values for human biomonitoring. Project number 59 000

Survey of interactions between different endocrine axes in aquatic test organisms (literature review). Project number 68 006

Federal Institute for Occupational Safety and Health (BAuA)
Histopathological examination of samples from a long-term inhalation study. Research project F 2325

Polycyclic aromatic hydrocarbons – Implementation of the concept of exposure-risk-relationships in enterprises handling strong polluted materials (ParKoURs); Effectiveness of organizational protective measures: efficacy comparison of different methods for cleaning work clothing. Research project F 2346, enhancement 518373

Comparison of inhalation and instillation as testing methods for characterization of granular biopersistent particles (GBP). Research project F 2364

Human exposure to biocidal products: Measurement of inhalation and dermal exposure during the application of biocide foams. Research project F 2366

Mode of toxic action of nanocarbons. Research project F 2376

Federal Institute for Risk Assessment (BfR)
Subacute in-vivo toxicity study in male rats with six structurally representative pyrrolizidine alkaloids

Subacute in-vivo toxicity study with pesticides in female rats as part of the Euro-Mix project

Federal Ministry for Economic Affairs and Energy
Central innovation program for SMEs – FINAMI
Development of an accelerated life cycle test for active implants

Federal Ministry of Education and Research (BMBF) framework program "Gesundheitsforschung" (health research)
Joint research project: 4-IN
Insect-derived inhalable inhibitors of bacterial virulence for treating lung infections

Joint research project: ANTI-TB
Antibiotic nanocarrier for inhalation treatment of tuberculosis

Joint research project: Phage4Cure
Developing bacteriophages as approved therapy against bacterial infections

Federal Ministry of Education and Research (BMBF) funding program "Alternatives to Animal Testing"
Project: InhalAb
Alternative models for testing of inhalable antibiotics

Federal Ministry of Education and Research (BMBF) funding program "Ersatz und Ergänzungsmethoden zum Tierversuch" (alternatives and complements to animal experiments)
Project: ExITox2 – Explain Inhalation Toxicity 2
Animal-free mechanism-based toxicity testing – predict toxicity after repeated dose inhalation exposure by using a read across approach

Federal Ministry of Education and Research (BMBF) funding program "Innovative Stammzelltechnologien für die individualisierte Medizin" (innovative stem cell technologies for individualized medicine)
Project: iCARE
Induced pluripotent stem cells for clinically applicable heart repair

Federal Ministry of Education and Research (BMBF) funding program NanoCare: "Auswirkungen synthetischer Nanomaterialien auf den Menschen" (impact of synthetic nanomaterials on human health)
Project: InhalT90
90-day inhalation testing with CeO_2 in the rat and subsequent analysis of gene expression profiles for the early detection of toxic/carcinogenic effects

Project: NanoCOLT
Long-term effect of modified carbon black nanoparticles on healthy and damaged lungs

Project: CaNTser
Investigation of the toxic potency of carbon nanotubes following long time inhalation

Federal Ministry of Education and Research (BMBF) project "Förderung von Forschungsstrukturen mit Argentinien, Brasilien, Chile, Kolumbien und Mexiko" (support of collaborative research structures with Argentina, Brazil, Chile, Colombia, and Mexico)
International Hearing Research
Establishment of a Chilean-German center of hearing medicine and research

Federal Office for Radiation Protection
Experimental analysis of emissions and radiological consequences after transportation accidents with surface-contaminated objects (SCO)

German Center for Lung Research (DZL)
Allergy and asthma
Chronic obstructive pulmonary disease (COPD)
Diffuse parenchymal lung diseases (DPLD)

Lower Saxony Ministry of Science and Culture
Joint research project: TransPlaMed
Establishment of distributed multicenter medical device prototype manufacturing with joint quality and risk management

Statutory Accident Insurance (DGUV)
Evaluation of usability of the physical characteristics of endogenously generated exhaled aerosols in the diagnosis of occupational lung diseases

International

CEFIC-LRI project: N5-FRAU
Histopathology of rats exposed to Barium sulfate nanoparticles by life-time inhalation exposure – Effects and Biokinetics

EFSA project: Applying a tested procedure for the identification of potential emerging chemical risks in the food chain to the substances registered under Reach – REACH 2

EU project: ERA-Net TRANSCAN
Analysis of tumor evolution and identification of relapse-initiating tumor cells in non-small cell lung carcinoma

EU project: Eurostars TARGIT
Development of next-generation treatment for allergies: targeted glycan-allergen immunotherapy

EU project: ICONS – Integrated Cooperation On Nanotube Safety
An integrated testing strategy for mechanistically assessing the respiratory toxicity of functionalized multi-walled carbon nanotubes

EU project: Innovative Medicines Initiative (IMI-2) – eTransafe
Enhancing translational safety assessment through integrative knowledge management

EU project: PHOENIX
Synergic combination of high-performance flame retardant nanolayered hybrid particles as real alternative to halogen-based flame retardant additives

EU project: PLATOX
In-vitro and in-vivo investigations to generate validated toxicity data of graphene nanoplatelets vs. a carbon black reference

EU project: PneumoNP
Nanotherapeutics to treat antibiotic-resistant Gram-negative infections of the lung

EU project: SILIFE
Production of quartz powders with reduced crystalline silica toxicity

EU project: ToxRisk (HORIZON 2020)
An Integrated European 'Flagship' Programme Driving Mechanism-based Toxicity Testing and Risk Assessment for the 21st century

German Federal Ministry of Education and Research (BMBF) and Ministry of Research, Technology and Higher Education of the Republic of Indonesia (RISTEK): joint research program for the identification and use of natural substances from Indonesia for the development of new therapeutics
Joint research project: Triple-IN
Insect-derived anti-infectives from Indonesia

Cooperation partners

National

ALS Automated Lab Solutions GmbH, Jena

Assay.Works, Regensburg

Augsburg University Hospital

BASF, Ludwigshafen

Bayer, Berlin

BioMedVet Research GmbH, Walsrode

Blackrock Microsystems Europe GmbH, Hannover

Boehringer Ingelheim Pharma GmbH & Co. KG

Cardior Pharmaceuticals GmbH, Hannover

Cellex Patient Treatment GmbH, Dresden and Cologne

Center of Allergy & Environment (ZAUM), Munich

Charité – Universitätsmedizin Berlin

Charité Research Organisation GmbH, Berlin

Cinfa Biotech GmbH, Munich

Clausthal University of Technology

Cortec GmbH, Freiburg

Cytena GmbH, Freiburg

ECT Oekotoxikologie GmbH, Flörsheim a. M.

Epomedics GmbH, Göttingen

Essen University Hospital

EurA Consult AG, Hamburg Office

EURICE – European Research and Project Office GmbH, Saarbrücken

European Aviation Safety Agency (EASA), Cologne

Federal Environment Agency, Berlin and Dessau

Federal Institute for Occupational Safety and Health (BAuA), Berlin and Dortmund

Federal Institute for Risk Assessment (BfR), Berlin

Federal Office for Radiation Protection (BfS), Salzgitter

FOBIG, Forschungs- u. Beratungsinstitut Gefahrstoffe GmbH, Freiburg

Forschungszentrum Jülich

Fraunhofer Institute for Applied Solid State Physics IAF, Freiburg

Fraunhofer Institute for Cell Therapy and Immunology IZI, Leipzig

Fraunhofer Institute for Chemical Technology ICT, Branch ICT-IMM, Mainz

Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB, Stuttgart and Würzburg

Fraunhofer Institute for Manufacturing Engineering and Automation IPA, Stuttgart

Fraunhofer Institute for Manufacturing Technology and Advanced Materials IFAM

Fraunhofer Institute for Material and Beam Technology IWS, Dresden

Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Schmallenberg

Fraunhofer Institute for Silicate Research ISC, Würzburg

Fraunhofer Institute for Surface Engineering and Thin Films IST

Freie Universität Berlin

Friedrich Schiller University Jena

GATC Biotech, Konstanz

GEMoaB Monoclonals GmbH, Dresden

GeneXplain GmbH, Wolfenbüttel

GenXPro GmbH, Frankfurt

German Aerospace Center (DLR), Cologne

German Cancer Research Center (DKFZ), Heidelberg

German Center for Infection Research (DZIF)

German Center for Lung Research (DZL)

German Primate Center, Göttingen

Gesellschaft für Anlagen- und Reaktorsicherheit (GRS), Cologne

Hannover Clinical Trial Center (HCTC), Hannover

Hannover Medical School

Heidelberg University

Helmholtz Center for Infection Research, Braunschweig

Helmholtz Zentrum München – German Research Center for Environmental Health, Munich

Heraeus Medical GmbH, Wehrheim

Hyglos GmbH, Bernried

Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA), Sankt Augustin

IPA – Institute for Prevention and Occupational Medicine of the German Social Accident Insurance at Ruhr-Universität Bochum, Bochum

Karlsruhe Institute of Technology, Division of Combustion Technology at the Engler-Bunte Institute, Karlsruhe

Kiel University

Leibniz-Institut für Analytische Wissenschaften – ISAS – e. V., Dortmund

Leibniz Institute DSMZ – German Collection of Microorganisms and Cell Cultures, Braunschweig

Leibniz Institute for Solid State and Materials Research (IFW), Dresden

Leibniz Research Centre for Working Environment and Human Factors (IfADo), Dortmund

Leibniz University Hannover

Ludwig-Maximilians-Universität München (LMU), Munich

LungenClinic Grosshansdorf GmbH

Merz Pharma GmbH & Co. KGaA, Frankfurt am Main

Molecular Networks, Nürnberg

Ostbayerische Technische Hochschule Regensburg

Otto Bock HealthCare GmbH

PharmaInformatic, Emden

Research Center Borstel

Robert Bosch GmbH – Packaging Technology, Crailsheim

RWTH Aachen

Sanum Kehlbeck GmbH & Co. KG, Hoya

Technische Universität Braunschweig

Technische Universität München (TUM), Munich

TRAIN – biomedical translation alliance in Lower Saxony, Hannover

TRON – Translational Oncology at the University Medical Center of the Johannes Gutenberg University, Mainz

TWINCORE (center for experimental and clinical research on infections), Hannover

Ulm University

Universitätsklinikum Erlangen

Universitätsmedizin Göttingen

University Hospital Carl Gustav Carus, Dresden

University Medical Center Hamburg-Eppendorf (UKE)

University of Applied Sciences and Arts, Göttingen

University of Cologne

University of Düsseldorf

University of Freiburg

University of Giessen

University of Leipzig

University of Lübeck

University of Marburg

University of Regensburg

University of Tübingen

University of Veterinary Medicine Hannover, Foundation

Vakzine Projekt Management GmbH, Hannover

Wacker Silicones, Munich

International

Adenium Biotech, Copenhagen (Denmark)

Advanced Bionics AG, Stäfa (Switzerland)

AIT Austrian Institute of Technology GmbH (Austria)

Altamira, Dayton, Ohio (USA)

Angle plc, Guildford (UK)

AstraZeneca (Sweden)

Brains On-Line (The Netherlands)

CeMM – Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna (Austria)

Cosmetics Europe, Brussels (Belgium)

Daiichi Sankyo, Tokyo (Japan)

Erasmus Medical Center, Rotterdam (The Netherlands)

European Food Safety Authority (EFSA), Parma (Italy)

Fraunhofer USA – Center for Molecular Biotechnology, Newark, Delaware (USA)

Fundación CIDETEC (CID), San Sebastián (Spain)

GlaxoSmithKline Research and Development Ltd., Brentford (UK)

Griffith University, Gold Coast (Australia)

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HANSABIOMED Ltd., Tallinn (Estonia)

IBMCC (Instituto de Biología Molecular y Cellular del Cáncer), Salamanca (Spain)

Instituto de Tecnología Cerámica, Castellón (Spain)

International Agency for Research on Cancer (IARC), Lyon (France)

IT'IS Foundation for Research on Information Technologies in Society, Zurich (Switzerland)

Izmir Biomedicine and Genome Center, Izmir (Turkey)

Johannes Kepler University Linz, Linz (Austria)

King Mongkut's University of Technology Thonburi (KMUTT), Bangkok (Thailand)

KU Leuven, Leuven (Belgium)

Leiden University, Leiden (The Netherlands)

Life Sciences Queensland, Brisbane (Australia)

Liverpool John Moores University, Liverpool (UK)

Maastricht University, Maastricht (The Netherlands)

Massachusetts Institute of Technology, Cambridge, Massachusetts (USA)

McMaster University Medical Center, Hamilton, Ontario (Canada)

Medical University of Graz, Graz (Austria)

Menarini Biomarkers (Singapore)

Menarini Silicon Biosystems, Bologna (Italy)

NordicBioscience (Denmark)

Novartis (Switzerland)

PExA, Gothenburg (Sweden)

RIVM National Institute of Public Health and the Environment, Bilthoven (The Netherlands)

Sahlgrenska University Hospital, Gothenburg (Sweden)

Stanford University School of Medicine, Stanford, California (USA)

TNO (The Netherlands)

Unilever (UK)

University of Alberta, Alberta (Canada)

University of Amsterdam, Amsterdam (The Netherlands)

University of Basel, Basel (Switzerland)

University of Bern, Bern (Switzerland)

University of Groningen, Groningen (The Netherlands)

University of Leeds, Leeds (UK)

University of Siena, Siena (Italy)

University of Southampton, Southampton (UK)

University of Utah, Salt Lake City, Utah (USA)

University of Utrecht, Utrecht (The Netherlands)

US Environmental Protection Agency (EPA), Chapel Hill, North Carolina (USA)

US WorldMeds, LLC, Louisville, Kentucky (USA)

Weizmann Institute of Science, Rehovot (Israel)

World Health Organization (WHO), Geneva (Switzerland)

Yale University, New Haven, Connecticut (USA)

Exhibitions, congresses and workshops

Fraunhofer ITEM presents its research and the services offered at national and international congresses and exhibitions. In addition, the institute organizes a variety of seminars and workshops. In 2017, the institute hosted or played an active role in the following events:

January 19-20, 2017
16th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany)

January 30-31, 2017
DZL Annual Meeting
6th annual conference of the German Center for Lung Research
Munich (Germany)

March 3-6, 2017
AAAAI 2017
Annual meeting of the American Academy of Allergy, Asthma and Immunology
Atlanta, Georgia (USA)

March 6-9, 2017
DGPT Annual Conference 2017
83rd annual conference of the German Society of Pharmacology and Toxicology (DGPT)
Heidelberg (Germany)

March 12-16, 2017
SOT 2017
56th annual meeting of the Society of Toxicology; including Fraunhofer ITEM exhibitor-hosted sessions on "Optimized testing of nanomaterials: a case report" and "Integrated approaches for inhalation toxicity assessment"
Baltimore, Maryland (USA)

March 22-25, 2017
DGP Congress 2017
58th annual congress of the German Respiratory Society (DGP)
Stuttgart (Germany)

April 3-4, 2017
European Coatings Show Conference 2017
Nürnberg (Germany)

April 4-6, 2017
in-cosmetics Global 2017
London (UK)

April 5-6, 2017
DBT 2017
German Biotech Days
Hannover (Germany)

April 6-7, 2017
2nd Joint Symposium on Nanotechnology
Hannover (Germany)

May 7-11, 2017
SETAC Europe 2017
27th European annual meeting of the Society of Environmental Toxicology and Chemistry
Brussels (Belgium)

May 19-24, 2017
ATS 2017
International conference of the American Thoracic Society
Washington, D.C. (USA)

June 3-7, 2017
21st ISAM Congress
Congress of the International Society for Aerosols in Medicine
Santa Fe, New Mexico (USA)

June 7-9, 2017
PCMG 2017
Annual conference of the Pharmaceutical Contract Management Group
Copenhagen (Denmark)

June 17-24, 2017
EAACI 2017
European Academy of Allergy and Clinical Immunology congress
Helsinki (Finland)

June 18-22, 2017
ICCE 2017
16th International Conference on Chemistry and the Environment
Oslo (Norway)

June 19-22, 2017
BIO International Convention 2017
San Diego, California (USA)

June 24-29, 2017
STP 2017
36th annual meeting of The Society of Toxicologic Pathology (STP)
Montreal (Canada)

July 21-25, 2017
ISMB/ECCB 2017
25th Conference on Intelligent Systems for Molecular Biology and 16th European Conference on Computational Biology
Prague (Czech Republic)

August 20-24, 2017
10th World Congress on Alternatives and Animal Use in the Life Sciences (WC10)
Seattle, Washington (USA)

August 29 – September 2, 2017
ESTP Congress 2017
Congress of the European Societies of Toxicologic Pathology (ESTP)
Lyon (France)

September 9-13, 2017
ERS Congress 2017
International congress of the European Respiratory Society
Milan (Italy)

September 10-13, 2017
EUROTOX 2017
53rd congress of the European Societies of Toxicology
Bratislava (Slovakia)

September 11, 2017
XV. Niedersächsischer Life Science Tag
15th Lower Saxony life science day
Braunschweig (Germany)

September 19-22, 2017
Eurobiofilms 2017
Amsterdam (The Netherlands)

September 25-27, 2017
InhaledParticles XII
Glasgow (UK)

October 17, 2017
Fresenius conference "Biozide: Bewertung und Zulassung"
Cologne (Germany)

October 25-27, 2017
AIT Annual Conference 2017
Copenhagen (Denmark)

October 26-27, 2017
Cosmetics Europe Science Conference 2017
Brussels (Belgium)

November 6-8, 2017
BIO-Europe 2017
Berlin (Germany)

November 9, 2017
Workshop "Environmental Risk Assessment of Veterinary Medicinal Products – Update, Recent Developments and Implications"
Hannover (Germany)

November 24, 2017
25th BVMA symposium
Munich (Germany)

Awards

In 2017, Fraunhofer ITEM researchers were awarded the following prizes for their scientific work:

Dr. Martin Hoffmann
Prize: Poster prize for the best poster in the "TransMed COSI" (TransMed = Translational Medicine, COSI = COmmunity of Special Interest) at ISMB/ECCB 2017.
Prize for the presented poster entitled "Modeling cellular evolution during lymph node colonization in melanoma patients", awarded on July 25, 2017 at the ISMB/ECCB Annual Conference 2017 (Intelligent Systems for Molecular Biology and European Conference on Computational Biology) in Prague (Czech Republic).

Prof. Dr. Christoph Klein
Prize: Gerhard Domagk Prize 2017
Prize awarded by the Gerhard Domagk Foundation in cooperation with the University Society of the University of Münster (Germany) for pivotal findings on mechanisms of early metastatic spread in breast cancer, awarded on December 8, 2017 in the Gerhard Domagk Institute for Pathology in Münster (Germany).

Prof. Dr. Antje Prasse
Prize: Poster prize 2017 of the German Respiratory Society (DGP).
Prize for the presented poster entitled "Molekulare Bildgebung mittels CXCR4-Gallium-68-Pentixafor PET erweist sich als ein geeigneter Biomarker im Therapie-monitoring der idiopathischen Lungenfibrose (IPF)", awarded on March 23, 2017 at the DGP Annual Congress in Stuttgart (Germany).

EDITORIAL NOTES

Coordination and editorial work
Dr. Cathrin Nastevska

Translation
Karin Schlemminger

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CONTACTS

Dr. Cathrin Nastevska
Public Relations
Phone +49 511 5350-225
cathrin.nastevska@item.fraunhofer.de

Annegret Seehafer
Marketing
Phone +49 511 5350-402
annegret.seehafer@item.fraunhofer.de

Fraunhofer ITEM
Headquarters
Nikolai-Fuchs-Strasse 1
(main entrance: Stadtfelddamm)
30625 Hannover
Germany
Phone +49 511 5350-0
Fax +49 511 5350-155

Fraunhofer ITEM
Pharmaceutical Biotechnology
Inhoffenstrasse 7
38124 Braunschweig
Germany
Phone +49 531 6181-6001
Fax +49 531 6181-6099

Fraunhofer ITEM
Personalized Tumor Therapy
Biopark 1
Am Biopark 9
93053 Regensburg
Germany
Phone +49 941 298480-23

Further information: www.item.fraunhofer.de