

# Particles & Health 2021

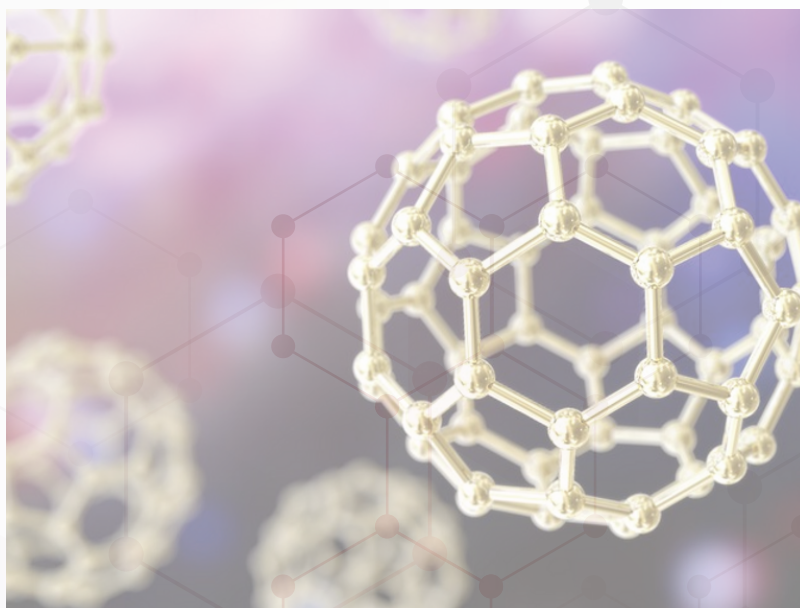
20th & 21st October  
Programme

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# CONTENTS

Contents .....	1
Background & Conference Goals .....	2
Schedule - Wednesday 20th October .....	3
Schedule - Thursday 21st October .....	4
Conference Speakers .....	5,6
Moderators & Scientific Partner.....	7
Sponsor - Institute of Occupational Medicine (IOM) .....	8, 9
Notes pages .....	10, 11



Conference supported by a grant from the International Carbon Black Association

# BACKGROUND

Regulatory initiatives in the European Union (EU) have resulted in proposed classifications for all poorly soluble low toxicity particles (PSLTs) for carcinogenicity. Examples of PSLTs include carbon black, titanium dioxide and iron oxide, among others. Approaches have also been proposed for setting workplace exposure limits for these materials, such as by the German MAK Commission.

This scientific conference will facilitate interaction and discussions among attendees with expertise in toxicology, epidemiology, occupational and pulmonary medicine and exposure assessment. The purpose of this conference is to promote interactions between these different disciplines to aid in the sound and evidence-based scientific underpinning of regulatory standard considerations regarding PSLTs. Although regulatory concern regarding PSLTs has focused on lung cancer risk as a result of rat inhalation overload studies, this conference will address all relevant health end points, including genetic and reproductive issues as well, consistent with ECHA guidelines.

Scientific Program Committee

Robert McCunney MD, MPH (Chair), Nathan Baker, Len Levy PhD, Kevin Driscoll PhD, Paul Borm PhD, Nils Krueger DVM, Dominique Lison MD, PhD, Lang Tran PhD, Rodger Duffin PhD, Vicki Stone PhD

## CONFERENCE GOALS

- Address scientific studies regarding human health effects of PSLTs. The value of human studies over animal studies-when human-exposed populations can be studied adequately- will be emphasized.
- Review and discuss definition of PSLT's proposed at Edinburgh workshop and published in 2020 in the Journal Inhalation Toxicology with attention to both similarities and differences among these substances.
- Address translational toxicology challenges, including the appropriateness of rats as models for human lung pathogenesis (particularly lung cancer) in light of lung overload phenomena and species differences.
- Serve as a platform to present current scientific information about PSLTs important for regulatory action.
- Publication of pertinent conference presentations in the peer reviewed scientific literature will allow the presentations to live beyond the conference and subsequently be reviewed part of regulatory deliberations.
- Establish an interdisciplinary setting for industry, academia and regulatory professionals to interact on an important topic. Such interaction can facilitate enhanced understanding of the science and appropriate classification, labeling and setting exposure limits, among others.
- Recommend areas for further research regarding the significance of the rat as a model for translation toxicology.
- Review the biokinetics of inhaled nanoparticles and the potential for non-pulmonary effects.

# WEDNESDAY 20TH OCTOBER

Human Studies

Session Chair: Rob McCunney, MD, MPH

Theme: Role of human studies, including epidemiology, in assessing health risk

9am	IOM and particles: a long history in research and service in protecting human health	Nathan Baker
	Role of epidemiology in human risk assessment	Ken Mundt, PhD
	Carbon Black and Lung Cancer Mortality – A Meta-regression Analysis Based on Three Occupational Cohort Studies	M.Yong, MD, PhD
	Coal and mortality	Robert McCunney, MD, MPH, MS
10.30am	Break	
10.50am	PSLT's & Lung Function and Malignancy: Causal Inference Analysis	Phil Harber, MD, MPH
	Pulmonary Inflammation, asthma and exhaled nitric oxide	Chris Fanta, MD
11.30am	Moderated by Robert McCunney, MD, MPH, MS Panelists. Robert Blink PhD, MD PSLT's and lung cancer; What do the epidemiology and human inhalation studies tell us?	
12.30pm	Lunch	
1.00pm	Luncheon Address: MEDICAL PUBLISHING TODAY Editor: Journal of Occupational and Environmental Medicine	Paul W. Brandt-Rauf, MD, ScD

Animal Studies

Session Chairs: Paul Borm, PHD, Alison Elder, PhD

Theme: Inflammation as a key adverse outcome pathway in particle induced effects

2.00pm	Macrophages, inflammation and lung cancer in 2021	Dominique Lison, MD, PhD
	Rat lung cancer, clearance overload and human health hazard - outcome of Edinburgh Expert Workshop	Kevin E. Driscoll, PhD
	Inflammatory pathways in humans-a broader perspective	Roger Duffin, PhD
	Pulmonary Cell Proliferation: The Missing Link in PSLTP-induced Lung Cancer. A pathologist's perspective	Jack Harkema, DVM, PhD, DACVP, ATSF
3.30pm	Break	
	Theme: Challenges provided by GHS based target organ toxicity-design and interpretation of inhalation studies of new and existing materials	
3.50pm	Pathology to be reconsidered? Oral and inhalation studies	Klaus Weber, PhD
	Wrap up and Summary	Alison Elder, PhD
	Moderated by Paul Borm, PhD and Alison Elder, PhD Panelist. Ann Hubbs, DVM, PhD A sample of questions: Is pulmonary inflammation the key adverse effect? Are sub chronic animal studies adequate? Are effects noted adaptive or adverse?	

# THURSDAY 21ST OCTOBER

Nanoparticle toxicology non-pulmonary effects

Session Chairs: Kevin Driscoll, PHD, Annie Jarabek, PHD

9.00am	Nanotechnology and health	Vicki Stone, PhD
	Toxicokinetics of Inhaled Nanoparticles	Otto Creutzenberg, PhD
	Dose- and Dosi-Metric Aspects and Biokinetics of Inhaled Poorly Soluble Low Toxicity (PSLT) Particles in Lung Overload	Günter Oberdörster, DVM, PhD
	In vivo Processing of Nanoparticles – Influence on Toxicity	Uschi Graham, PhD
10.30am	Break	
10.50am	Genotoxicity of multi-walled carbon nanotube reference materials in mammalian cells and animals	Peter Møller, PhD
	Neurotoxicity of Nanoparticles	Roel Schins, PhD
	Reproductive and developmental toxicity	Karin Sørig Hougaard, PhD, MSc, BM, ERT
	Occupational exposure to carbon black and risk of cardiovascular disease	Robert McCunney, MD, MPH
	Wrap up and Summary	Kevin Driscoll, PhD Annie Jarabek, PHD

12.30pm	Lunch	
1.00pm	Luncheon Address Microplastics and Health: A new challenge for regulators and scientists	Stephanie Wright, PhD

Regulatory Application of Science

Session Chairs: Len Levy, OBE, PHD, Nils Krueger, PHD, DVM

2.00pm	Regulatory application of science to Particles and Health - some introductory observations	Len Levy, OBE, PhD
	Regulatory application of science and stakeholder engagement - setting EU Occupational Exposure Limits	Alick Morris
	Testing materials in a world of reduced emphasis on animal testing; OECD Guidelines	Thomas Kuhlbusch
	Applying Translational Science Approaches to Protect Workers Exposed to Nanomaterials	Paul Schulte, PhD
3.30pm	Break	
3.50pm	Can we reduce animal testing- tiered approach using in-vitro screening?	Martin Wiemann, PhD
	NanoScreen: Assessing the impact of SAS particles on advanced in -vitro intestine models	Peter Wick
	Acute Inhalation Toxicity Part 1: The challenge to create particulate aerosols for acute toxicity testing – a systematic approach	Jürgen Nolde, PhD
	Acute Inhalation Studies Part 2: Non-specific particle effects now trigger classification?	Nils Krueger, PhD, DVM
	Moderated by Len Levy, OBE, ,PhD, Nils Krueger, PhD, DVM Panelist: Tim Bowmer, Alick Morris, Paul Schulte, PHD Discussion Topics: The art of regulation; what the regulators need from the scientists Putting regulatory decisions into practice to protect workers, involving stakeholders Non-specific inflammatory responses as a basis for classification? Adaptive and reversible effects as triggers for regulation? Can we predict effects without further animal studies? Can we move away from rodents for effects in the lung-better use of human and in vitro data?	
	Closing Comments	Nathan Baker, Robert McCunney, MD, MPH

# SPEAKERS



Vicky Stone, PhD  
TOPIC: Nanotechnology and health  
AFFILIATION: Heriot-Watt University



Nathan Baker  
TOPIC: IOM and particles; a long history in researched service and to protect human health  
AFFILIATION: IOM



Robert McCunney, MD, MPH  
TOPIC: Human Health  
AFFILIATION: Harvard Medical School



Dr. Chris Fanta, MD  
TOPIC: Pulmonary Inflammation, asthma and exhaled nitric oxide  
AFFILIATION: Harvard



Peter Møller, PhD  
TOPIC: Genotoxicity  
AFFILIATION: University of Copenhagen



M. Yong, MD, PhD  
TOPIC: Meta-analysis of carbon black cohort mortality studies  
AFFILIATION: University of Dusseldorf



Peter Wick  
TOPIC: NANOSCREEN  
AFFILIATION: EMPA, Switzerland



Ken Mundt, PhD  
TOPIC: Role of epidemiology in human risk assessment  
AFFILIATION: Ramboll



Otto Creuzenberg, PhD  
TOPIC: Toxicokinetics of inhaled nanoparticles  
AFFILIATION: Fraunhofer ITEM



Alison Elder, PhD  
TOPIC: Animal Studies  
AFFILIATION: University of Rochester



Rodger Duffin, PhD  
TOPIC: Inflammatory pathways in humans - a broader perspective  
AFFILIATION: University of Edinburgh



Günter Oberdörster, DVM, PhD  
TOPIC: Does metrics-mass, size, surface, composition: What really matters?  
AFFILIATION: University of Rochester



Kevin E. Driscoll, PhD  
TOPIC: Rat lung cancer and human hazard  
AFFILIATION: Rutgers



Karin Sørig Hougaard, PhD, MSc, BM, ERT  
TOPIC: Reproductive and developmental toxicology  
AFFILIATION: University of Copenhagen

# SPEAKERS



Uschi Graham, PhD  
TOPIC: In Vivo processing of nanoparticles - influence on toxicity  
AFFILIATION: Topasol LLC



Roel Schins, PhD  
TOPIC: Nanoparticle toxicology - Non-pulmonary effects  
AFFILIATION: Leibnitz Research Institute for Environmental Medicine



Alick Morris  
TOPIC: Regulatory application of science  
AFFILIATION: DG Employment



Thomas Kuhlbusch  
TOPIC: Testing materials in world of reduced emphasis of animal testing  
AFFILIATION: BAuA/OECD



Paul W. Brandt-Rauf, MD, ScD  
TOPIC: Medical publishing today  
AFFILIATION: Dean Drexel University SPH



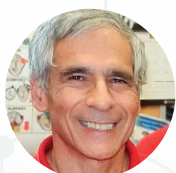
Dominique Lison, MD, PhD  
TOPIC: Macrophages, inflation and lung cancer  
AFFILIATION: University Louvain



Jack R. Harkema, DVM, PhD, DACVP, ATSF  
TOPIC: Pulmonary cell proliferation - the missing link?  
AFFILIATION: Michigan State



Stephanie Wright, PhD  
TOPIC: Microplastics and Health: A new challenge for regulators and scientists  
AFFILIATION: Kings College



Philip Harber, MD, MPH  
TOPIC: Accelerated decline in lung function  
AFFILIATION: University of Arizona



Paul Schulte, PhD  
TOPIC: Applying translation science approaches to protect workers exposed to nanomaterials  
AFFILIATION: NIOSH



Len Levy OBE, PhD  
TOPIC: The regulators dilemma - an introduction  
AFFILIATION: Cranfield University



Martin Wiemann, PhD  
TOPIC: Can we reduce animal testing? Tiered approach using in-bitro screening  
AFFILIATION: Institute for Lung Health



Jürgen Nolde, PhD  
TOPIC: The challenge to create particulate aerosols for acute toxicity testing – a systematic approach  
AFFILIATION: DIR. Product Stewardship/Grace Europe Holding



Klaus Weber, PhD  
TOPIC: Pathology to be reconsidered? Oral and inhalation studies  
AFFILIATION: ANNAPATH  
AFFILIATION: Institute for Lung Health

# MODERATORS



Paul Borm, PhD

Moderator of Animal Studies



Robert Blink, PhD

Moderator of Human Studies



Robert McCunney, MD,  
MPH, MS

Moderator of Human Studies



Nils Krueger, PhD, DVM

Moderator of Regulatory  
Application of Science



Alison Elder, PhD

Moderator of Animal Studies



Len Levy, OBE, PhD

Moderator of Regulatory Applica-  
tion of Science



Kevin E. Driscoll, PhD

Moderator of Nanoparticle  
toxicology -Pulmonary and  
Non-pulmonary challenges



Annie Jarabek, PhD

Moderator of Nanoparticle  
toxicology - Non-pulmonary  
Effects

# SCIENTIFIC PARTNER



Nathan Baker  
Chief Executive Officer  
Institute of Occupational Medicine (IOM)



# Supporting you

The Institute of Occupational Medicine (IOM) helps you to create safe environments. IOM brings together multi-disciplinary expertise in hazard, exposure and risk assessment, using current best practice and international standards for particle measurement, toxicology, occupational hygiene and risk management. To do this effectively we can help you with:



## RISK ASSESSMENTS

Undertaking risk assessment is an essential part of complying with your regulatory obligations. IOM helps organisations in understanding the risks, offering advice and ensuring that staff are protected. Our team can provide:

- Risk assessments through integration of hazard and exposure evaluations, with recommendations on safe practice and appropriate control measures;
- Reviews to scope, assess and interpret evidence and emerging issues;
- Evidence appraisal to inform policy, guidance and standards development;
- Development of workplace exposure limits and safety datasheets;
- Advice and support to ensure you comply with regulations.



## WORKPLACE EXPOSURE MONITORING OF PARTICLES AND NANOMATERIALS

To undertake risk assessment an understanding of the levels of exposure, potential releases and control is needed to protect workers. Our approach is tailored to the detection and characterisation of airborne particulates that can pose a health risk.

We can identify and help you control exposure in the workplace through:

- Real-time characterisation of particle release from the handling, manufacture and finishing of products and articles;
- Background monitoring to discriminate between natural and process-related emissions;
- Personal and area sampling of airborne particles, with off-line gravimetric, imaging, and/or chemical analysis;
- Evaluation of control measures;
- Providing comprehensive analysis, interpretation, and best practice recommendations.

## HAZARD ASSESSMENT & TOXICOLOGY TESTING

A thorough understanding of health hazards of new materials, as well as defining hazard paradigms for well-established products, allows new products, ideas and innovations to be explored and swiftly brought to market.

Our knowledge and expertise

of particle toxicology provides the hazard information you need to safely develop and market materials and products whilst also meeting regulatory requirements.

We can help you through every step of the process:

- Benchmarked in vitro toxicology

studies for inhalation, dermal, and ingestion exposure;

- Sample preparation and characterisation;
- Customised study designs for particles and fibres, assessing key markers for cellular stress.

## LABORATORY SERVICES & ANALYSIS

IOM offers a number of specialist laboratory services to support the risk assessment of particles, including:

- Particle aerosolisation with in situ characterisation of number, size and surface area,
- Sampling for off-line microscopy,

gravimetric and chemical analysis by ICP-AES;

- Particle fractionation to provide respirable-size-classified samples for toxicity assessments;
- Dustiness testing to European Standard EN 15051;

- Biodurability assessment;
- Morphological and elemental sample analysis by SEM/ EDXS;
- Particle density measurement by Helium pycnometry;
- Measurement of size distribution and surface charge (by laser diffraction and zeta-potential);

## INDEPENDENT RESEARCH SUPPORT

When it comes to investigating current issues, understanding new materials and improving policy, IOM's research group is on hand to help you. Trusted by the EU, UK governments and other notable institutions we are committed to delivering independent and impartial research. We provide authoritative evidence-based

research, which informs policy. Our areas of expertise include:

- Environmental & Occupational exposure science
- Nanosafety
- Air Pollution (Indoor and Outdoor)
- Chemical Exposure & Risk Assessment

- Work related Health & Wellbeing
- Toxicology
- Human factors, Psychology & Ergonomics.

IOM can investigate issues, offer independent guidance and provide informed solutions. Allow us to help you find the solutions to your challenges today.

## CONTACT OUR EXPERTS



**Dr Matthew Boyles**  
SAFENANO Senior Toxicologist



**Dr Karen Galea**  
Research Team Lead



**Prof Lang Tran**  
Principal Computational Toxicologist



**William Brown**  
Research Team Lead



**Carolyn McGonagle**  
Head of Chemistry

## GET IN TOUCH

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