39th International MEDICHEM Congress on Occupational and Environmental Health in the Production and Use of Chemicals

Heidelberg, Germany
2 - 5 June 2011
# Program at a Glance

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<th>Thursday, June 2</th>
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<tr>
<td><strong>9.00</strong> Departure of Bus from Marriott Hotel: Excursion to BASF SE, Ludwigshafen (the Cradle of MEDICHEM; optional)</td>
<td><strong>8.15</strong> Welcome and Introduction</td>
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<td><strong>10.25</strong> Case Reports – Interesting observations in the occupational health world</td>
<td><strong>10.25</strong> Lunch – Poster / Exhibition</td>
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<td><strong>11.20</strong> Toxicology – New results, emerging risks</td>
<td><strong>12.15</strong> Tea / Coffee – Poster / Exhibition</td>
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<td><strong>15.30</strong> Registration, Handing over of Posters and Presentations</td>
<td><strong>15.35</strong> Regulation in occupational health – Recent developments and REACH – Impact on occupational and environmental health (cont.)</td>
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<tr>
<td><strong>18.00</strong> Opening Ceremony with Welcome Addresses, Music, Cold and Warm Buffet and Opening of Exhibition</td>
<td><strong>16.15</strong> - <strong>16.50</strong> Strategic Approach to International Chemicals Management (SAICM) – Status and developments</td>
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<td><strong>18.00</strong> Church of the Holy Spirit (Heilig Geist Kirche), Organ Concert with Wenzel Hübner (Entrance from 17.45 to 18.15, then door will be closed)</td>
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<td><strong>22.00</strong> Ca. End</td>
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<td><strong>12.30</strong> Lunch (optional)</td>
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<tr>
<td><strong>14.00</strong> Adverse effects on employees, customers and the general public – Preventive measures</td>
<td><strong>13.00</strong> Closing of Conference</td>
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<td><strong>16.00-17.00</strong> MEDICHEM General Assembly</td>
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<td><strong>18.00</strong> Departure of Bus from Marriott Hotel to Heidelberg Castle</td>
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<td><strong>19.00</strong> Reception, Gala Dinner and Giant Fireworks at Heidelberg Castle</td>
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<td><strong>23.00</strong> First Bus to Marriott Hotel</td>
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<td><strong>23.45</strong> Last Bus to Marriott Hotel</td>
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www.medichem2011.org
Dear Colleagues,

we are happy today to welcoming you at the 39th International MEDICHEM Congress on Occupational and Environmental Health in the Production and Use of Chemicals, held in Heidelberg, Germany, from 2 – 5 June 2011.

25 years after the last congress in Germany in 1986 you followed our cordial invitation to return to the cradle of MEDICHEM, which was founded by Prof. Alfred Thiess in Ludwigshafen in 1972. At the invitation of BASF SE, the congress starts with an excursion to BASF in Ludwigshafen near Heidelberg (optional). High-ranking representatives from Politics, Industry, Trade Unions and Academia will be welcoming you at the official Opening Ceremony on Thursday evening.

With an A-List of brilliant speakers we intend to provide scientific excellence and exchange of knowledge on cutting-edge developments in all fields concerned. They will be discussing the challenges and finding solutions together with you, the participants of the premier 2011 International Health Event in Heidelberg, within the different topics of the MEDICHEM 2011 Theme: Occupational Health in a Changing World.

MEDICHEM’s prime objective is international co-operation on those occupational and environmental health issues of universal concern related to the production and use of chemicals that are most effectively resolved through a globally co-ordinated approach. MEDICHEM promotes the exchange of information and ideas between all those involved: Occupational health physicians, occupational hygienists, epidemiologists, toxicologists, environmental and safety specialists, occupational health nurses, regulators, and students in these fields. To be able to provide this unique and only complete programme for global experts in these fields we offered you the platform: You followed our invitation to submit abstracts for free oral or poster presentations.

In choosing the Marriott Hotel we are convinced that we are offering you all conceivable comforts of a most convenient congress venue. During the breaks you will have direct access from the conference room to the waterside terrace, where you can relax and talk to colleagues. Lunch will be served in the water-side Mediterranean restaurant. To give many participants the convenience of on-site accommodation at the congress venue, the modern and comfortable 5-star Marriott Hotel, situated on the banks of the Neckar River, is offering you a sensational special discount rate of 118 Euro for single rooms, including breakfast buffet and use of the pool. All those who registered and booked early will have the additional privilege, at no extra charge, of staying in one of the rooms overlooking the Neckar.

The City of Heidelberg, with its romantic townscape is an event in itself. The city is also home to Germany’s oldest university which will be celebrating its 625th anniversary in 2011. The harmonious ensemble of the world-famous castle ruins, the Old Town and the Neckar river nesting among the hills inspired the painters and poets of 19th century Romanticism. The city’s fascination continues until today for millions of visitors from all over the world.

With the conference fee of 590 Euro, which also includes the social events, we hope to satisfy participants who have an active working life. To give a possibility for our retired colleagues to join the congress we offered a reduced fee for them of 250 Euro, all-inclusive. The congress social events (all included in the conference fee) will feature the Opening Ceremony, framed by music, with cold and warm buffet reception on Thursday, an organ concert in the Church of the Holy Spirit in the heart of Heidelberg’s famous Old Town and the reception by the Mayor of Heidelberg at the Town Hall just opposite the church on Friday, as well as the Champagne reception on the Castle Gallery, the Gala Dinner in the Castle, and the Giant Firework display on Saturday.

With this all-inclusive conference package we hope that all participants will not only benefit from a productive and profitable congress but also enjoy a few memorable days in Heidelberg in the early summer of 2011.

A very warm welcome to all participants, sponsors and exhibitors at MEDICHEM 2011!

Heidelberg, May 20, 2011

Thomas Köhler, Maren Beth-Hübner, Alfred Thiess

Thomas Köhler (Managing Director BG RCI)
Dr. Maren Beth-Hübner (Chair, Organizing and Scientific Committees MEDICHEM 2011)
Prof. Dr. Alfred Thiess (Founder & Honorary President of MEDICHEM)
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<tr>
<td>Bonjour</td>
<td>French</td>
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<tr>
<td>Salam Ale Kom</td>
<td>Iranian</td>
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<td>Herzlich Willkommen!</td>
<td>German</td>
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<td>Gruetzi</td>
<td>Swiss German</td>
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<td>Huan Ying</td>
<td>Chinese</td>
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<td>aap ka swaagat hein</td>
<td>Hindi</td>
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<td>haere mai</td>
<td>Maori (New Zealand)</td>
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<td>Salaam</td>
<td>Arabic</td>
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<td>Ulwamkelo</td>
<td>Xhosa (South Africa)</td>
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<td>Groeten</td>
<td>Dutch</td>
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<td>Barukh Habayim</td>
<td>Hebrew</td>
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<td>Walcum</td>
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<td>Härzläch wellkomm</td>
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<td>Шчыра запрашаем</td>
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Thursday, June 2, 2011

9.00  Departure of bus from Marriott Hotel

Excursion to BASF SE, Ludwigshafen
(the cradle of MEDICHEM; optional)

15.00  Return to Marriott Hotel

17.00  Registration, Handing over of posters and presentations

18.00  Opening Ceremony

Heidelberg Brass Orchestra, Welcome Drink

Moderation: Dr. Maren Beth-Hübner Chair of the Organizing and of the Scientific Committees of MEDICHEM 2011, BG RCI (German Social Accident Insurance Institution for the Raw Materials and Chemical Industry) Heidelberg, Germany

Theresa Bauer The Minister of Science, Research and the Arts of Baden-Württemberg, Germany

Dr. Joachim Gerner Mayor of the City of Heidelberg, Germany

Prof. Dr. med. Dr. h. c. Alfred M. Thiess Founder and Honorary President of MEDICHEM, Ludwigshafen, Germany. Member of the Organizing and of the Scientific Committee of MEDICHEM 2011

Heidelberg Brass Orchestra
Dr. Eggert Voscherau Chairman of the Supervisory Board of BASF SE, Ludwigshafen, Germany

Michael Vassiliadis President of the Industrial Union of Mining, Chemical and Energy (IG BCE), Hannover, Germany

Dr. Gerd Romanowski Executive Director of the Chemical Industry Association (VCI), Frankfurt, Germany

Heidelberg Brass Orchestra

Thomas Köhler Managing Director BG RCI (Berufsgenossenschaft Rohstoffe und chemische Industrie; German Social Accident Insurance Institution for the Raw Materials and Chemical Industry, formerly BG Chemie), Member of the Organizing Committee of MEDICHEM 2011, Heidelberg, Germany

Opening of Cold and Warm Buffet and Opening of Exhibition

Heidelberg Brass Orchestra

22.00 Ca. End
Friday, June 3, 2011

8.15 Welcome of the Chair of the Executive Committee of the MEDICHEM Board  
*Dr. Thirumalai Rajgopal* Vice President, Global Medical & Occupational Health, Unilever, India

8.20 Welcome by the host, BG RCI  
*Thomas Köhler* Managing Director BG RCI, Heidelberg, Germany

8.35 Introduction into the scientific program (Invited Speaker)  
*Prof. Dr. Heidi Foth* Director of the Institute of Environmental Toxicology  
Martin-Luther University Halle-Wittenberg, Halle / Saale, Germany

8.50 – 9.55  
**Shift work and cancer – Current discussion**  
Chair:  
*Dr. Michael Nasterlack*  
Vice President,  
Occupational Medicine & Health Protection, BASF SE, Ludwigshafen, Germany  
and  
*Dr. Abed bin Onn*  
Subang Jaya Selangor, Malaysia

8.50 **KEYNOTE: The carcinogenicity of shift work – The IARC evaluation and beyond**  
*Prof. Dr. Kurt Straif* Head of the Section of the IARC Monographs,  
International Agency for Research on Cancer (IARC), World Health Organization (WHO), Lyon, France

9.15 **Shift work and cancer: Principles, perspectives and Pitfalls of "white-box" epidemiology**  
*Prof. Dr. Thomas C. Erren* Director and Chair, Institute and Policlinic for Occupational Medicine, Environmental Medicine and Prevention Research, University of Cologne, Germany

9.35 **Shift work and cancer – State of science and practical consequences**  
*Dr. Michael Nasterlack* (Invited Speaker) Vice President, Occupational Medicine & Health Protection, BASF SE, Ludwigshafen, Germany

9.55 **Tea / Coffee and Poster / Exhibition viewing**
10.25 – 11.20

Case Reports – Interesting observations in the occupational health world

Chair:

Dr. Andreas Flückiger
Head of Roche’s Corporate Health Protection Department
Hoffmann-La Roche Ltd., Basel, Switzerland

and

Dr. Diane J. Mundt
ENVIRON International Corporation, Boston, USA

10.25 Can epigenetics affect occupational health? – An overview
Dr. Amir Radfar Babol University of Medical Sciences, Babol, Iran
Granting the MEDICHEM Young Professionals Award

10.40 Evaluation of work-related psychosocial and ergonomic factors in relation to low back discomfort in emergency unit nurses
Prof. Dr. Ehsan Habibi Isfahan University of Medical Sciences, Isfahan, Iran
Granting the MEDICHEM Young Professionals Award

10.55 Exposure to ethyl methane sulfonate in a pharmaceutical: Risk assessment for patients and workers
Dr. Andreas Flückiger (Invited Speaker) Head of Roche’s Corporate Health Protection Department, Hoffmann-La Roche Ltd., Basel, Switzerland

11.20 – 12.15 / 13.45 – 14.15

Toxicology – New results, emerging risks

Chair:

Prof. Dr. Günter Oberdörster
Professor of Toxicology
Department of Environmental Medicine, University of Rochester
Director of the University of Rochester-EPA Ultrafine Particle Center
Head of the Pulmonary Core of the NIEHS Center Grant Rochester, Rochester, USA

and

Dr. Kenneth A. Mundt
Principal and Director of Epidemiology
ENVIRON International Corporation, Boston, USA

11.20 KEYNOTE: Environmental Toxicology – New results, emerging risks
Dr. Avi Wiener Medical Director, Institute of Occupational & Environmental Medicine, Rambam Medical Center, Haifa, Israel
11.45  Aberrant methylation and expression of tumor suppressor gene p15 and p16 in benzene poisoning
Dr. Caihong Xing  National Institute of Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention, Beijing, China
Winner of the MEDICHEM Scholarship Award

12.00  Utilizing the pH 6.7 Syrian hamster embryo (SHE) cell transformation assay to predict the carcinogenic potential of aromatic amines
Dr. Sabine Plöttner  Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of Ruhr University Bochum (IPA), Bochum, Germany

12.15  Lunch and Poster / Exhibition viewing

13.45  Dose-response at very low exposures: Biological rhymes and reasons
Dr. Annette B. Santamaria  ENVIRON International Corporation, Houston, Texas, USA

14.00  Censored exposure (dose) data: Challenges for the occupational hygienist, toxicologist and epidemiologist
Frederick Boelter  Principal, ENVIRON International Corporation, Chicago, Illinois, USA
14.15 – 15.05 / 15.35 – 16.15

Regulation in occupational health – Recent developments
and

REACH – Impact on occupational and environmental health

Chair:

Prof. Dr. Andrea Hartwig
(Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area)
Professor at the Karlsruhe Institute of Technology (KIT)
Institute of Applied Biosciences, Department of Food Sciences and Toxicology, Karlsruhe, Germany

and

Prof. Dr. Heidi Foth
Director of the Institute of Environmental Toxicology
Martin-Luther University Halle-Wittenberg, Halle / Saale, Germany

14.15  KEYNOTE: The concept of SCOEL to set OELs

Prof. Dr. Helmut Greim
Member of SCOEL (Scientific Committee on Occupational Exposure Limits), Member of the Risk Assessment Committee of ECHA (European Chemicals Agency in Helsinki, Finland), Institute of Toxicology and Environmental Hygiene, Technical University, Munich, Germany

14.40 The role of expert judgement and conceptional approaches in setting OELs by the German MAK Commission

Prof. Dr. Andrea Hartwig  (Invited Speaker)
President of the "MAK-Commission" (Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area), Professor at the Karlsruhe Institute of Technology (KIT), Institute of Applied Biosciences, Department of Food Sciences and Toxicology, Karlsruhe, Germany

15.05 Tea / Coffee and Poster / Exhibition viewing

15.35 Labelling of hazardous chemicals under GHS

Dr. Helmut Fleig
Helmut Fleig Consulting, Mannheim, Germany

15.50 Occupational Exposure Limits and REACH

Dr. Gisela Stropp  (Invited Speaker)
Head, Institute for Toxicology, Department of Product Stewardship Industrial Chemicals & Operations at Bayer Schering Pharma AG, Chairperson of the subcommittee on "Hazard Risk Assessment" of the German Advisory Committee on Hazardous
16.15 – 16.50
Strategic Approach to International Chemicals Management (SAICM) – Status and developments
Chair:
Prof. Dr. Maged Younes
Director Food Safety, World Health Organization (WHO), Geneva, Switzerland
Former Head UNEP (United Nations Environment Programme), Chemicals Branch, Geneva, Switzerland
and
Prof. Dr. Helmut Greim
Member of SCOEL (Scientific Committee on Occupational Exposure Limits)
Member of the Risk Assessment Committee of ECHA
(European Chemicals Agency in Helsinki, Finland), Munich, Germany

16.15 KEYNOTE: Introduction: Management of chemicals: The global context
Prof. Dr. Maged Younes Director Food Safety, World Health Organization (WHO), Geneva, Switzerland. Former Head UNEP (United Nations Environment Programme), Chemicals Branch, Geneva, Switzerland

16.30 South Africa – International conventions (ILO, REACH), local legislative framework, best practice and biological monitoring: A 25 years perspective. What can we learn from this for developing countries? (Invited Speaker)
Dr. William Murray Coombs Dow, Regional Health Director - Middle East, Africa & India, Sentrachem Limited, Bryanston; South African Society of Occupational Medicine, South Africa

18.00 Church of the Holy Spirit (Heiliggeistkirche), Organ Concert with Wenzel Hübner
(Entrance from 17.45 to 18.15, then door will be closed)

19.00 Palais Prinz Carl, Kornmarkt 1, Reception with the Mayor of the City of Heidelberg Wolfgang Erichson

21.30 Ca. End
Saturday, June 4, 2011

8.30 – 10.00 / 10.30 – 12.30
Nanotechnology – Challenges and solutions

**Chair:**
*Prof. Dr. Dr. Uwe Heinrich*
Head of Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Hannover, Germany

and

*Dr. Maren Beth-Hübner*
BG RCI (German Social Accident Insurance Institution for the Raw Materials and Chemical Industry), Department of Hazardous Substances and Biological Agents at Work, Heidelberg, Germany

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8.30 **KEYNOTE: Nanotoxicology, a challenge for nanotechnology**

*Prof. Dr. Günter Oberdörster* Professor of Toxicology, Department of Environmental Medicine, University of Rochester, Director of the University of Rochester-EPA Ultrafine Particle Center, Head of the Pulmonary Core of the NIEHS Center Grant Rochester, Rochester, USA

9.00 Nanotechnology - Challenges for and solutions via inhalation toxicology

*Prof. Dr. Dr. Uwe Heinrich (Invited Speaker)* Head of Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Hannover, Germany

9.30 Responses to pulmonary exposure to nanoparticles in NIOSH animal studies

*Dr. Vincent Castranova (Invited Speaker)* NIOSH (National Institute for Occupational Safety and Health), Chief of the Pathology and Physiology Research Branch, Morgantown, USA

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10.00 **Tea / Coffee and Poster / Exhibition viewing**

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10.30 Studies on the carcinogenicity of carbon nanotubes

*Prof. Dr. Ken Donaldson (Invited Speaker)* Director of the Edinburgh Lung and Environment Group Initiative (ELEG) Laboratory, Queen’s Medical Research Institute, MRT Centre for Inflammation Research, University of Edinburgh, Edinburgh, Scotland, UK

11.00 Evaluation of nanoparticles by the German MAK-Commission: Current status and research needs

*Prof. Dr. Andrea Hartwig (Invited Speaker)* President of the "MAK-Commission" (Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area), Karlsruher Institute of Technology (KIT), Karlsruhe, Germany
11.30 Exposure assessment strategies of engineered nano-materials in the workplace and implementation to the industrial practice

Dr. Stefan Engel BASF SE, Hazardous Chemicals Management, Ludwigshafen; Chair, Working Group on Exposure to Nanomaterials in the Workplace of BAuA, BG RCI, IFA and VCI, Germany

11.50 Occupational health and safety at handling and use of carbon nano tubes

Dr. Jacques Ragot Bayer Material Science AG, Global Product Stewardship, Leverkusen, Germany

12.10 Exposure control: Prudent practices at the workplace

Dr. Thomas H. Brock (Invited Speaker) Head, Department of Hazardous Substances and Biological Agents at Work, BG RCI (German Social Accident Insurance for the Raw Materials and Chemical Industry), Heidelberg, Germany

12.30 Lunch and Poster / Exhibition viewing

14.00 – 15.00 / 15.30 – 16.00
Adverse effects on employees, customers and the general public – Preventive measures

Chair:
Dr. Michael Nasterlack
Vice President, Occupational Medicine & Health Protection, BASF SE, Ludwigshafen, Germany

and

Dr. William Murray Coombs
Dow, Regional Health Director - Middle East, Africa & India, Sentrachem Limited, Bryanston, South Africa

14.00 Ototoxic substances at the workplace

Dr. Eberhard Nies Head, Toxicology of Industrial Chemicals, Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA), Sankt Augustin, Germany

14.15 The European social dialogue on crystalline silica – A sustainable agreement in occupational health

Dr. Karlheinz Guldner VBG (Verwaltungs-Berufsgenossenschaft), Würzburg, Germany

14.30 Occupational health during the decommissioning of mercury cells plants

Dr. Jean-Claude Besson Arkema, Euro Chlor, Saint-Fons, France
(presented by Dr. Michael Nasterlack Vice President, Occupational
14.45 Particulate matter (PM) in new technology diesel exhaust (NTDE) is distinctly different from traditional diesel exhaust (TDE)

*Dr. William B. Bunn* Vice President - Health, Safety, Security and Productivity, Navistar, Inc., Professor In Preventive Medicine, Northwestern University School of Medicine, Chicago, USA

15.00 *Tea / Coffee and Poster / Exhibition viewing*

15.30 Working environment control over lead toxicity at ceramics powderdust manufacturing factory

*Dr. Keiichi Fujimoto* Osaka Medical College, Department of Hygiene and Public Health, Osaka, Japan

Granted the MEDICHEM Young Professionals Award

15.45 Chemical ocular burns: Experimental data and clinical implications

*Prof. Dr. Norbert Schrage* Head of Ophtalmology Department, University Hospital Köln-Merheim, Köln, Germany

16.00 MEDICHEM General Assembly

17.00

18.00 Departure of bus from Marriott Hotel to Heidelberg Castle

19.00 Reception, Gala Dinner and Giant Fireworks at Heidelberg Castle

23.00 First bus to Marriott Hotel

23.45 Last bus to Marriott Hotel
Sunday, June 5, 2011

8.30 – 10.15 / 10.45 – 11.30
Biomarkers – Progress in research and practical application

Chair:
Dr. Heiko U. Käfferlein
Head of Centre of Toxicology, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance Institute of Ruhr University Bochum (IPA), Bochum, Germany

and
Dr. Martina Piasek
Institute for Medical Research and Occupational Health, Zagreb, Croatia

8.30 KEYNOTE: Aromatic amines and bladder cancer – Current and future biomarkers for health preventive measures
Dr. Heiko U. Käfferlein Head, Centre of Toxicology, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of Ruhr University Bochum (IPA), Bochum, Germany

8.50 Uroscreen - Tumor markers for early detection of bladder cancer in chemical workers
Dr. Beate Pesch Head, Centre of Epidemiology, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of Ruhr University Bochum (IPA), Bochum, Germany

9.10 Biomarkers of metal exposure and their effects in women of childbearing age in Zagreb Ccounty, Croatia
Dr. Martina Piasek Institute for Medical Research and Occupational Health, Zagreb, Croatia
Winner of the MEDICHEM Scholarship Award

9.25 Protein adduct analysis after short-term exposure to alkylating chemicals – Examples, prospects, limitations
Dr. Michael Bader BASF SE, Occupational Medicine & Health Protection, Ludwigshafen, Germany

9.40 Assessing chemical exposures to improve health
Prof. Dr. Rupali Das Chief, Exposure Assessment Section, Environmental Health Branch, California Department of Public Health, Richmond, USA
9.55  Effects of vapours and aerosols of bitumen on biomarkers of inflammation – Assessment of irritative effects on the airways of mastic asphalt workers using non-invasive methods
Prof. Dr. Monika Rauf-Hheimsoth  Head, Centre of Allergology/Immunology, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr University Bochum (IPA); Bochum, Germany

10.15  Tea / Coffee and Poster / Exhibition viewing

10.45  Novel approach for the biomonitoring of occupational exposure to 2-chloroprene
Priv. Doz. Dr. Thomas Göen  Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine (IPASUM), University of Erlangen-Nuremberg, Erlangen, Germany

11.00  Occupational exposure to mercury in oil and gas platforms: Confounding effects of seafood intake in biomonitoring of blood
Prof. Dr. Salmaan H. Inayat-Hussain  University Kebangsaan Malaysia, Kuala Lumpur, Malaysia

11.15  Simulation of blood and urine levels with a generic PBTK-model in MS-excel following inhalation and/or oral uptake and/or dermal exposure
Dr. Frans Jongeneelen  IndusTox Consult, Nijmegen, Netherlands

11.30 – 12.40
Occupational health – Trends and evolution
Chair:
Dr. Steffen Hitzeroth  Medical Director Occupational Health Procter & Gamble Service GmbH, Schwalbach a. Ts., Wiesbaden, Germany
and
Dr. Andreas Flückiger  Head of Roche's Corporate Health Protection Department Hoffmann-La Roche Ltd., Basel, Switzerland

11.30  KEYNOTE: Psychosocial risks at the workplace – An increasing challenge for health protection
Dipl.-Psych. Roland Portuné  BG RCI (German Social Accident Insurance Institution for the Raw Materials and Chemical Industry), Department of Occupational Psychology, Heidelberg, Germany

Sunday, June 5, 2011
11.50  Evolution of social protection systems for occupational and industrial risks  
Dr. Irina Filip  University of Medicine and Pharmacy Gr. T. Popa, Iasi, Romania

12.05  Development and pilot of a leading health metric scorecard for the UK chemical industry  
Dr. Alister J. Scott  Director of Group Health, Johnson Matthey PLC, Royston, Herts, UK

12.20  Unconventional threats to corporate leadership: General concepts of preparedness, recognition, and mitigation  
Dr. William L. Lang  Senior Director, Shoreland, Inc., Arlington, Virginia, USA. Former Medical Director at the White House, Washington, USA.

12.40  Promotion of MEDICHEM 2012 in Cancun, Mexico

12.45  Promotion of MEDICHEM 2013

12.50  Closing of Conference  
Thomas Köhler  Managing Director BG RCI, Heidelberg, Germany

13.00  Lunch (optional)
Case Reports – Interesting observations in the occupational health world

Occupational expositions to dangerous products in view of the Poisons Information Centre Freiburg, Germany

Dr. Uwe Stedtler Poisons Information Centre, Centre for Pediatrics and Adolescent Medicine, University Medical Centre, Freiburg, Germany

Toxicology – new results, emerging risks

Biological effects of europium (III) chloride hexahydrate in rats after single oral doses

Prof. Dr. Kan Usuda Osaka Medical College, Department of Hygiene and Public Health, Osaka, Japan
Regulation in occupational health – Recent developments
and
REACH – Impact on occupational and environmental health

The use of biological reference values for the exposure assessment of chemical substances at the workplace

Priv. Doz. Dr. Thomas Göen Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine (IPASUM), University of Erlangen-Nuremberg, Erlangen, Germany

Nanotechnology – Challenges and solutions

Cross-sectional and longitudinal studies of health effect markers among engineered nanomaterial exposed workers

Dr. Saou-Hsing Liou Division of Environmental Health and Occupational Medicine, National Health Research Institutes, Miaoli, Taiwan

Generating defined nanoparticles in an environmental friendly way for toxicology and inhalation experiments

Jürgen Spielvogel Palas GmbH, Karlsruhe, Germany
Adverse effects on employees, customers and the general public – Preventive measures

Study of association between job stress (based on job demands and control model) and cardiovascular disease risk factors among petrochemical company personnel

*Prof. Dr. Ehsan Habibi* Isfahan University of Medical Sciences, Isfahan, Iran

Sustainability and proactive product stewardship at Navistar

*Dr. William B. Bunn* Vice President - Health, Safety, Security and Productivity, Navistar, Inc., Professor in Preventive Medicine, Northwestern University School of Medicine, Chicago, USA

A new method of misbalance correction of ecologically mediated syndrome of increased chemical sensitivity in children and juveniles

*Dr. Nataly Pats* Grodno Medical University, Grodno, Belarus

Biomarkers – Progress in research and practical application

Mycotoxin screening method using a MTT cleavage assay for environmental and occupational health studies.

*Dr. Eckardt Johanning* Fungal Research Group Foundation, Inc./Johanning MD PC, Albany, New York, USA

Blood AhR activator levels and disease odds ratios in populations with high and background exposure to PCP waste

*Dr. Saou-Hsing Liou* Division of Environmental Health and Occupational Medicine, National Health Research Institutes, Miaoli, Taiwan
Occupational health – Trends and evolution

Haz-Map: A project to map occupational toxicology information into a relational database

Dr. Jay A. Brown Consultant, U.S. National Library of Medicine, Tacoma, USA
ABSTRACTS

(Alphabetical Order of Presenting Author)
Protein adducts are sensitive and specific biomarkers for a broad spectrum of reactive chemicals or their metabolites. While the basic assumption for the interpretation of adduct levels and for the setting of benchmark or reference values is a steady state condition of adduct formation and depletion, significantly increased adduct concentrations may also be observed after intermittent or short-term exposure.

An accidental exposure of six workers to ethylene oxide (EO) provided the rationale for a follow-up biomonitoring that was aimed on the observation of adduct kinetics and the differentiation between accidental and environmental exposure, e.g. by EO in tobacco smoke. For this purpose, the decrease in the concentration of the hemoglobin adduct of EO, N-2-hydroxyethylvaline (HEV), was followed during a six-months period after the accident, together with N-2-cyanoethylvaline (CEV) and urinary cotinine, two well-established biomarkers for smoking.

The follow-up study shows that EO adduct concentrations were raised after a short accidental exposure up into the range of formerly established benchmark values for repeated exposure (e.g. the German EKA correlation). The initial biomonitoring revealed HEV concentrations above 500 pmol/g globin in all cases, with a maximum of about 2400 pmol/g globin (EKA for 1 ppm EO: ~ 3900 pmol/g globin). The adduct levels dropped in accordance with the expected zero-order kinetics for a single exposure. After the six month observation interval, the HEV concentrations in blood reflected the individual exposure of the study participants to EO in tobacco smoke. The accompanying CEV and cotinine analyses confirmed the individual smoker status of the workers.

The results of this study as well as the prospects and limitations of the approach are discussed together with recent data on similar exposure situations (acrylonitrile, epichlorohydrin, formaldehyde), thus providing a basis for the application and interpretation of adduct measurements after short-term or accidental exposure.
CENSORED EXPOSURE (DOSE) DATA: CHALLENGES FOR THE OCCUPATIONAL HYGIENIST, TOXICOLOGIST AND EPIDEMIOLOGIST

Boelter, F. (1), Jones, R. M. (1), Poole, J. L. (2), Simons, C. E. (1)
(1) ENVIRON International Corporation, Chicago, Illinois, USA
(2) ENVIRON International Corporation, Tampa, Florida, USA

BACKGROUND AND OBJECTIVE: Incorporating exposure data that are below limits of detection into exposure assessments for toxicological and epidemiological evaluations of cumulative and aggregate human health risks.

METHODS: In four different studies, hundreds of data points were collected and analyzed and models were developed to characterize worker and/or community exposures where human health injury had been alleged. One study involved benzene from an oil spill, a second study involved asbestos exposure from gasket removal activities, a third study involved mixed chemical and physical agent exposure in semiconductor production, and a fourth study involved dioxin exposure from heavy pesticide application. In several of these studies, biological data also were gathered (i.e. urinary phenol correlated to benzene exposure). More than 80% of all the collected data were censored meaning analytical values were below limits of quantification. Kaplan Meier statistics, which are normally associated with survival analyses, have been recommended for left censored exposure data, especially where the lognormal distribution assumption cannot be verified. The Kaplan Meier estimates are basically non parametric estimates adjusted for the non detects, but the median and mean require that the fraction of censored data is less than 0.50 and for the 95th percentile that the fraction censored is less than 0.95. Because all of the datasets were censored, the geometric mean and geometric standard deviation were estimated using the Maximum Likelihood Estimation method.

RESULTS: Consistently, the exposure data analysis demonstrated exposures were less than 1/10th of the allowable daily exposure limit for a working lifetime. Many of the tasks examined were intermittent or non-recurring. Corresponding biological data showed less than 5% of allowable limit of, for example, urinary phenol. Combining exposure data results with information regarding time at task or time of exposure can yield useful information regarding dose.

CONCLUSION: Censored data sets provide challenges for the occupational hygienist, toxicologist and epidemiologist. Nevertheless, systematic examinations using quality data involving exposure and time allow for estimation of very low doses. Given reasonable understanding of biological modes of action, estimates of the probability of the risk for disease development may be derived or demonstrated epidemiologically.
EXPOSURE CONTROL: PRUDENT PRACTICES AT THE WORKPLACE

Brock, T. H. (1)
(1) BG RCI, Heidelberg, Germany

Great efforts have been put into research to enlighten the risks of nanotechnology. Still we do not know enough about the effects to quantify possible risks. Challenging as this is for future research a problem for occupational safety rises: How can we reduce the possible risks without a proper data basis?

Luckily enough we have positive answers to that. The strategy to manage the uncertainties is to reduce exposure ALARP, esp. against Nanomaterials. Having learned to install effective methods of exposure control for all kinds of substances with other hazardous substances over years we experience that they are working very effectively with nanoobjects too. Most of the produced nanoobjects (esp. particles, fibres, filaments, rods and tubes) are used as classical chemicals by mixing with matrices to achieve better or new properties of materials. An arsenal of safety measures is available for the production and the down-stream use. Even if the visions of K. Eric Drexler will be reality some day (this may stay fiction – on the other hand “some day” may be earlier than one thinks) technology to control exposures against self-reproducing entities is available as well: these methods are well-proven in microbiology and genetic engineering.

We can chose from laboratory fume cupboards to glove boxes, from closed systems to proper ventilation of machinery and work places, from respiratory protection to proper gloves. Typically in R&D we will work in fume cupboards or laminar flow benches with a exposure almost zero. A variety of ventilation techniques is available for exposure control of machines and apparatus (high-performance mills e. g.). Working in closed systems is also a technology well-established in chemistry for decades. Also important determinants for the effectiveness is not only the use of proper equipment and the avoidance of contaminations but – even more – the proper use itself. Even with a gold standard for the technical measures: training of the users on proper use and personal behaviour is crucial for a minimum of exposure.

Better safe than sorry! This can be achieved with not too great an effort by applying well-known prudent practices.
HAZ-MAP: A PROJECT TO MAP OCCUPATIONAL TOXICOLOGY INFORMATION INTO A RELATIONAL DATABASE

Brown, J. A. (1)
(1) National Library of Medicine, Tacoma, WA, USA

Haz-Map is a relational database of occupational toxicology that has been freely accessible on the website of the National Library of Medicine since 2002. The goal of Haz-Map is to collect into one database the best information available regarding occupational exposures and diseases. Haz-Map was designed to improve access to information and to support the early recognition and prevention of work-related diseases.

This is a project to index and map the knowledge domain of occupational toxicology starting with the big picture and then adding the details. The two levels of information in the database are toxicity (chemicals) and hazards (diseases). The seven main tables in the database are Chemicals, Industrial Processes, Home Activities, Occupational Diseases, Signs & Symptoms, Hazardous Job Tasks, and Occupations. All of the tables are linked so that queries can be performed to show all diseases that match a job AND a symptom or all chemicals that match an adverse effect AND an industrial process. There are 225 occupational diseases in the database. Each disease is linked to symptoms, hazardous job tasks, and causative chemicals.

Since 2006 the number of chemical profiles in the database has jumped from 1400 to 5800. In the past year, the author added 22 fields to the Agents table to capture animal data from systematic and summarized monographs recently published by both the Environmental Protection Agency (EPA) and the Organisation for Economic Co-operation and Development (OECD). In the next few years, the author plans to add more chemicals, to revise existing profiles, and to make Haz-Map a more useful resource for occupational health and safety professionals.
The proactive product stewardship program at Navistar Inc. is making progress in three major areas of sustainability: environmental, social, and economic. To address these three areas, the company has focused on reducing the environmental impacts of its operations and products, while at the same time promoting local community goals, creating favorable workplace environments, and providing economic rewards for reducing greenhouse gases. Environmental sustainability seeks to meet or exceed the regulatory mandate on emissions of air pollutants from products, including heavy-duty diesel engines using a combination of innovative product designs and proactive implementation of emissions reduction technologies. In addition, Navistar has continued to investigate the human health implications of exposure to diesel exhaust, a complex mixture that changes considerably with technology advances. To be socially sustainable, Navistar strives to be beneficial to the health and welfare of both employees and communities in areas where Navistar has facilities. The company is striving to be more economically sustainable by increasing energy efficiency at its manufacturing facilities and of its products, thereby saving money for the both the company and the customers. Factoring environmental, health, safety, security, and local community goals into business decisions benefits both society at large as well as the company. Establishing a reputation for socially responsible business practices creates goodwill among key stakeholder groups, and makes the company more attractive to high quality employees. Socially responsible investors may be more attracted to the company, and a sustainability strategy may also provide a competitive advantage for product marketing over other companies, to the extent that customers care about the environmental and social record of companies.
PARTICULATE MATTER (PM) IN NEW TECHNOLOGY DIESEL EXHAUST (NTDE) IS DISTINCTLY DIFFERENT FROM TRADITIONAL DIESEL EXHAUST (TDE)

(1) Navistar, Inc., Chicago, IL, USA
(2) Gradient, Inc., Cambridge, USA
(3) Lapin and Associates, Glendale, USA

Diesel exhaust (DE) characteristic of pre-1988 engines was classified as a "probable" human carcinogen (Group 2A) by the International Agency for Research on Cancer (IARC), and the US Environmental Protection Agency has concluded that DE is "likely to be carcinogenic to humans." These classifications were based on the large body of health effect studies conducted on DE over the past 30 or so years. However, increasingly stringent US emissions standards (1988 to 2010) for particulate matter (PM) and nitrogen oxides (NOx) in diesel exhaust have helped stimulate major technological advances in diesel engine technology and diesel fuel and lubricant composition, resulting in the emergence of what has been termed New Technology Diesel Exhaust, or NTDE. NTDE is defined as DE from an advanced technology (post-2006) diesel engine, which consists of an integrated system of advanced engine designs, exhaust aftertreatment configurations, and reformulated fuel and lube oil. Numerous emissions characterization studies have demonstrated marked differences in regulated and unregulated emissions between NTDE and what has become known as "traditional diesel exhaust" (TDE) from pre-1988 diesel engines. Now there exist even more data demonstrating significant chemical and physical distinctions between the diesel exhaust particulate (DEP) in NTDE versus TDE, and its greater resemblance to particulate emissions from compressed natural gas (CNG) or gasoline engines. Furthermore, preliminary toxicological data suggest that the changes to the physical and chemical composition of NTDE lead to differences in biological response between NTDE exposure versus TDE exposure. Ongoing studies are expected to address some of the remaining data gaps in the understanding of possible NTDE health effects, but there is now sufficient evidence to conclude that toxicity studies of pre-2007 DE likely have little relevance in assessing the potential health risks of NTDE exposures.
RESPONSES TO PULMONARY EXPOSURE TO NANOPARTICLES IN NIOSH ANIMAL STUDIES

Castranova, V. (1)
(1) National Institute for Occupational Safety and Health (NIOSH), Morgantown, West Virginia, USA

Carbon nanotubes (CNT) are being explored for applications as structural materials, for energy transmission and storage, for bone grafting, for dental implants, and for targeted drug delivery. Due to the wide array of commercial applications, inhalation exposure is possible during synthesis, use, and disposal of CNT. Therefore, adverse health effects in workers dealing with CNT are of concern. A growing body of scientific studies is being created concerning the pulmonary effects of lung exposure to single-walled carbon nanotubes (SWCNT) as well as multi-walled carbon nanotubes (MWCNT). Commonly reported pulmonary responses include:

1. rapid but transient elevation of pulmonary inflammation and damage;
2. rapid and persistent formation of inflammatory granulomatous lesions at deposition sites of agglomerated CNT structures;
3. rapid and persistent interstitial fibrosis associated with the migration of more dispersed CNT structures into alveolar septa.

Also of pulmonary concern is the ability of MWCT to translocate to the intrapleural space and the ability of SWCNT and MWCNT to disrupt normal mitosis, thus, raising the specter that CNT may cause mesothelioma and/or lung cancer. Pulmonary exposure has also been associated with dysfunction of the cardiovascular system (aortic plagues and failure of coronary arterioles to respond normally to dilators) and the brain (induction of mRNA for inflammatory mediators and markers of blood/brain barrier damage). In response to these scientific reports, the National Institute for Occupational Safety and Health (NIOSH) in the United States has conducted risk assessment and calculated benchmark lung burdens for rodent studies of CNT using pulmonary granulomas and interstitial fibrosis as adverse health endpoints. From these benchmark lung burdens, NIOSH has proposed a recommended exposure limit (REL) for CNT workers. These data and the methods used to develop a REL for CNT will be reviewed and discussed in this presentation.
SOUTH AFRICA - INTERNATIONAL CONVENTIONS (ILO, REACH), LOCAL LEGISLATIVE FRAMEWORK, BEST PRACTICE AND BIOLOGICAL MONITORING: A 25 YEARS PERSPECTIVE. WHAT CAN WE LEARN FROM THIS FOR DEVELOPING COUNTRIES?

Coombs, W. M. (1)
(1) Dow, Regional Health Director - Middle East, Africa & India, Sentrachem Limited, Bryanston, South Africa; South African Society of Occupational Medicine

A country rich in mineral resources with a long history of extractive industrial activity.

LOCAL LEGISLATION: South Africa has a rich, progressive and comprehensive occupational health legal history. The first mining health and safety laws predate the 20th century. Asbestos and health effects date back as far as 1924, with noise induced hearing loss, silicosis and asbestosis as the first recognized occupational diseases for compensation. The first compensation law dates to 1941. The “new era” from 1993 started with a complete review of Occupational Health (OH) legislation and a plethora of legislative requirements followed, not only for OH but also environmental and safety (now close to 140 acts and regulations exist) most notably the Machinery and Occupational Safety Act no.6 of 1983 and the Hazardous Chemical Substance Regulations 1993.

INTERNATIONAL AND LOCAL GOVERNANCE: During the latter part of the 20th century and 10 years into the 21st century South Africa is fully integrated into global OH governance and standards. International conventions, ILO and other, are now implemented as a matter of course. The Chemical Industry has responded likewise and the Responsible Care global programme has most of the activity around chemistry as signatories. CAIA (Chemical and Allied Industry Association) publishes annually on the results; Examples relevant to MEDICHEM will be shared

MEDICAL AND OCCUPATIONAL HEALTH PRACTICE: Results from 20 years for BM (now up to 60 000 samples per year) will be shared, noting that even with the extensive and comprehensive legislative requirements the levels from the BM dataset are not as low as would be predicted/expected.

CONCLUSION: The continual body burden of chemicals (organic and inorganic) may be due to several factors; long history of exposure (metals/asbestos) with long tails in disease patterns, underlying vulnerabilities (HIV, treatment of HIV, chronic disease, environmental, childhood exposures etc), continual exposure with absence of best practice in protection in particular respiratory protection (fit testing etc), lack of compliance testing/rigorous enforcement/workforce pressure and quality in laboratory/monitoring methodology, to name a few. Biological Monitoring may not be the best or only indicator of OH performance, in SA it may point to a long-term occupational disease case finding due to the continued body burdens. A call is made for working together with international agencies to develop an integrated approach (international database) to mitigate exposures, protect workers and lower body burdens. The Chemical Industry and MEDICHEM may be able to support.
ASSESSING CHEMICAL EXPOSURES TO IMPROVE HEALTH

Das, R. (1)
(1) California Department of Public Health (CDPH), Richmond, USA

For decades, biomonitoring has been used to evaluate and control exposures in the workplace, where it remains an important medical surveillance tool, albeit for a limited number of substances. The number of chemicals that can be biomonitored has substantially increased and the use of biomonitoring in non-occupational settings has expanded more rapidly than in workplaces. As a result, consumers have become aware that they may be exposed to chemicals through products of daily living and health care providers are grappling with issues of interpreting health impacts of low level exposures and recommending appropriate interventions. In an effort to improve health, in 2006, the state of California in the United States of America established Biomonitoring California, the nation’s first mandated biomonitoring program, to document levels and examine trends in exposures of the general public and workers to specific chemicals. This talk will describe Biomonitoring California and its achievements. Biomonitoring California is a collaboration of epidemiologists, laboratorians, toxicologists, and physicians. A Scientific Guidance Panel prioritizes for biomonitoring chemicals of greatest potential health importance for California’s population. Public input is encouraged and results must be returned to individuals who request them. Cohorts currently being biomonitored are mother-infant pairs and firefighters. Preliminary work is being conducted to include a statewide representative sample of the population. Analytes of interest include heavy metals; environmental phenols; brominated and chlorinated flame retardants; organochlorine, organophosphate, and pyrethroid pesticides; phthalates; and polychlorinated biphenyl compounds. Best practices are being developed for returning and interpreting results for substances where “normal” levels and adverse health impacts have not yet been definitively established. Biomonitoring California has two major practical applications. First, by engaging consumers, occupational and environmental physicians, and scientists, it will help to increase education and enhance appropriate use of biomonitoring. Additionally, it will provide data to programs, such as the Green Chemistry Initiative, to facilitate the formulation and manufacture of safer products, thereby preventing adverse health effects of chemical exposure in both workers and consumers.
In order to ensure safe use of carbon nanotubes we need to understand how they act in the body so that regulation can be focused on the harmful fraction (the biologically effective dose). We have been addressing the pathogenicity of long and short multi-wall carbon nanotubes (MWCNT) in relation to the unique hazard posed to the pleural mesothelium by asbestos fibres e.g. mesothelioma. There is persuasive evidence that a fraction of all deposited particles reach the pleura and that a mechanism of particle clearance from the pleura exists, through stomata in the parietal pleura. We therefore used injection into the pleural space as a model that mimics the true translocation of a fraction of deposited CNT to that site. We injected a panel of long and short carbon nanotubes (Poland et al Nature Nanotechnology 2008), into the pleural space of mice and followed the inflammatory and fibrogenic response. We found clear evidence of length-related inflammation in the pleural space with long amosite asbestos and two long nanotubes samples, while all the short fibres samples of asbestos and nanotubes failed to elicit significant inflammation. The response seen with long fibres is due to the retention of long fibres stomata on the parietal pleura whilst short fibres can negotiate the stomata and drain to the mediastinal lymph nodes. We have gone on to study a number of other nanofibres of different materials – silver nanowires and nickel nanowires and shown similar length-dependent inflammatory effects in the pleural space. Along with length, biopersistence of fibres is important in their pathogenicity and we have also examined the biopersistence of carbon nanotubes and found them to be biopersistent by the standard in vitro durability assay. Our studies suggest that nanofibres will adhere to the fibre pathogenicity paradigm that has so far predicted the pathogenicity of all fibres studied which describes the biologically effective dose for fibre type pathogenicity as being long, thin, biopersistent fibres.
EXPOSURE ASSESSMENT STRATEGIES OF ENGINEERED NANOMATERIALS IN THE WORKPLACE AND IMPLEMENTATION TO THE INDUSTRIAL PRACTICE

Engel, S. (1)
(1) BASF, Ludwigshafen, Chair of the Working Group on Exposure to Nanomaterials in the Workplace of BAuA, BG RCI, IFA and VCI, Germany

Engineered nanomaterials (ENMs) are fascinating, new materials with significantly improved or completely novel properties. They are being handled more and more in the workplaces both in research and in production. The Chemical Industry in Germany has subscribed to the Responsible Care Global Charter and is therefore committed to a safe, responsible and sustainable development of this highly promising technology. This includes appropriate organizational measures as well as the implementation of a high level of industrial hygiene standards. Amongst others, it has lead to the development of the Guidelines on the Responsible Use of Nanomaterials in the Workplace, jointly issued by the Federal Institute of Occupational Safety and Health (BAuA) and the German Chemical Industry Association (VCI) in 2007, which is currently under revision.

Currently no specific, binding, health-based exposure limits for aerosols containing ENMs in workplace operations have been established. However, a need exists for exposure and risk assessment of aerosols released from ENMs in workplace operations. The field of toxicology of ENMs is evolving and until substance specific, health-based occupational exposure limit values (OELs) have been established and validated it is common practice to apply a precautionary approach to mitigate exposure in the workplace to adequately protect the workforce. Efficient, reliable, but also pragmatic exposure assessment is a crucial element and the starting point for the effective management of risks potentially posed by hazardous chemicals in the workplace. Therefore, VCI established a working group to address and discuss the challenges of such exposure assessment, in particular of exposure assessment of aerosols released from ENMs in the workplace. The working group was interested in summarizing the current state-of-the-art, in establishing a pragmatic and widely usable exposure assessment strategy and in publishing case studies.

The literature review was commissioned to an author consortium of recognized experts in the field from the Institute of Energy and Environmental Technology (IUTA e.V.) in Duisburg and the Technical University of Dresden. The focus of the review was both, exposure related to workplace measurements and also laboratory testing of potential nanomaterial release. In total almost 250 literature references were identified and evaluated. Only about 25 publications were considered as being highly relevant. The review article will be published in a recognized peer-reviewed journal. Also a proposal for a harmonized exposure assessment strategy was developed in co-operation with the Federal Institute of Occupational Safety and Health (BAuA), German Social Accident Insurance Institution for the Raw Materials and Chemical Industry (DGUV-BG RCI) and Institute for Occupational Safety and Health of the DGUV (IFA). The outcome was supposed to be pragmatic and widely usable in the field, rather than to form the basis for further scientific and research oriented studies, e.g. epidemiological studies. A tiered-type approach, which can be widely used by small and medium size enterprises as well as large chemical companies with global business and operations was the result of the work.

In addition several case studies related to such exposure assessment are planned or have already been drafted and submitted by the Chemical Industry in Germany for peer-reviewed publication. The presentation will be based on the results of the VCI working group as outlined. Furthermore, it will also include results of the European research project NANODEVICE, which is developing portable, easy-to-use devices for exposure assessment of workplace aerosols containing ENMs. The talk will cover aspects of exposure assessment of workplace aerosols released from intentionally manufactured nanomaterials. Measurement of fine and ultrafine dust will not be in the scope of the talk.

The proposed exposure assessment strategy will be in the focus of the presentation. The presentation will give an overview on the current situation and introduce the possibilities and the challenges of exposure assessment of ENMs released into workplace air. Aspects of the exposure assessment will be illustrated with examples taken from literature or the case studies.
SHIFT WORK AND CANCER: PRINCIPLES, PERSPECTIVES AND PITFALLS OF "WHITE-BOX" EPIDEMIOLOGY

Erren, T. C. (1), Morfeld, P. (2)
(1) Institute and Policlinic for Occupational Medicine, Environmental Medicine and Prevention Research, University of Cologne, Germany
(2) Institute for Occupational Epidemiology and Risk Assessment (IERA), Essen, Germany

The 2007 IARC [International Agency for Research on Cancer] classification “Shift work that involves circadian disruption is probably carcinogenic to humans (Group 2A)” offers promising perspectives but also pitfalls for necessary epidemiological research in coming years.

On the one hand, the conundrum of possible links between shift work, circadian disruption or chronodisruption and internal cancers provides a unique case for “white-box” epidemiology: a series of biologically plausible causal mechanisms has been suggested and convincingly tested in experiments. Epidemiology will now have a key role to investigate diligently whether one or more of these tantalizing mechanisms are at work in shift workers or not. Importantly, future observational studies should become more effective as they can be disciplined and channelled by abundant biomedical insights.

On the other hand, strong experimental evidence should not mislead us to lower quality and replication standards of observational studies in this important research area. In this vein, a critical pitfall to avoid is that biological plausibility could be wrongly invoked to facilitate publication of observational research of inappropriate quality and validity. To the contrary, we must strive for "quality" studies and we will need appropriate replication (“quantity”) of epidemiological findings. To accompany strong experimental data with weak and uninterpretable epidemiological work will not suffice.

To contribute to the necessary series of "quality" studies, this presentation develops and discusses - with a critical reference to Ioannidis' "Why Most Published Research Findings are False" [PLoS Med 2005] - specific recommendations as to how epidemiological research into biologically plausible links between shift work and cancer should be (i) designed, (ii) reported and (iii) interpreted. To exemplify, studies should be primarily conducted where shift work actually occurs, i.e., at the workplaces where men and women are exposed to work regimes at unusual times but also to complex other occupational factors. Indeed, as population-based cohort and case-control studies will likely be hypothesis-generating, it will be important to have industry-based investigations, allowing us to consider occupational exposure data of appropriate detail, completeness and accuracy. Ultimately, detailed individual shift work histories that were/are collected in an independent fashion, rather than relying on post-hoc interview information, will be imperative to reliably assess - or exonerate - possible cancer risks for shift workers..
EVOLUTION OF SOCIAL PROTECTION SYSTEMS FOR OCCUPATIONAL AND INDUSTRIAL RISKS

Filip, I. (1), Radfar, A. (2), Asgharzadeh Ahmadi, S.A., (2)
(1) University of Medicine Gr. T. Popa, Iasi, Romania
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Over about the last two decades, with economic globalization and the development of new technologies, the working world has undergone multiple changes which demands occupational risk insurance and social protection.

Fast development of the service economy has also brought changes to the nature of work related injuries in both developed and developing world. The occupational injuries and accidents alternatively, cause much harm not only to the individuals but also put an extra burden on the community and state economy. Governments, NGOs, and international organizations historically have been providing services, policy and legislative guidance on occupational health and safety for their beneficiaries. The challenge however, is, not only to identify new risks but also to find out how to cope with them at regional and global level in both developing and developed world.

In this review article, on the basis of historical background, samples of social security systems (pertaining to occupational health) from developed and developing countries, nongovernmental, international organizations who are providing policy and legislative guidance on occupational health and safety have been described.

KEY WORDS: Occupational Injuries, Social Security, Workers Compensation, Occupational Health and Safety.
LABELLING OF HAZARDOUS CHEMICALS UNDER GHS

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The overall objective of all Chemicals Safety Programs is the direct or indirect protection of human beings, i.e. of workers, general population/consumers and of the environment. In order to be able to handle and use hazardous (dangerous) chemicals safely, the potential hazards must be known and communicated in an appropriate way. Hazard Communication has been performed since decades basically via two instruments: Labelling on the packaging and Safety Data Sheets, but with distinctly diverging systems. The GHS, the "Globally Harmonized System of Classification and Labeling of Chemicals" has been developed since 1992 by international organisations like OECD and endorsed by the UN in 2003. The new system has been or is being implemented in many regions of the world, e.g. in the EU (CLP Regulation (No) 1272/2008; 31 December 2008), in Japan and probably soon in USA. In the EU, substances marketed after 1 December 2010 and preparations/mixtures after 1 June 2015 have to be labelled according to the new CLP system (Classification, Labelling and Packaging). The relevant new or modified GHS-Labelling Elements are: GHS Pictograms; Signal Words; Hazard- and Precautionary Statements. They are coded to facilitate data processing. The "GHS Pictograms" convey hazards optically at a first glance; they are standardized graphical compositions which give specific information. There are altogether nine pictograms for Physical, Health and Environmental Hazards, e.g.

- Flame
- Exclamation Mark
- Health Hazard Pictogram

"Signal Words" indicate the relative level of severity of the hazard in order to alert the reader to a potential hazard on the label. There are two signal words: "Danger" for serious hazards, "Warning" for less serious hazards. "Hazard Statements" are assigned to a "Hazard Class" describing the nature of the Hazard (e.g. Flammable liquids or Acute toxicity) and to a "Hazard Category" reflecting the degree of severity within one hazard class (e.g. Acute toxicity: Categories 1-5, the highest figure representing the lowest degree). There are at the time being 71 H-statements exhibiting detailed information on the hazards. Examples are H 225 = "Highly flammable liquid and vapour" for Flam. liquids Category 2, H 300 = "Fatal if swallowed" for Acute oral toxicity Category 1, H312 = "Harmful in contact with skin" for Acute dermal toxicity Category 4. "Precautionary Statements" describe in a standardized manner necessary and/or recommended measures in order to prevent or minimize the adverse effects resulting from exposure. There are 127 P-statements from which pool the most appropriate ones should be chosen. Too many statements on a label could water down the warning effect and thus being counter-productive. With the knowledge of the product properties including physico-chemical ones and the intended uses, the number of P-statements can be reduced by using expert judgement. The P-statements have been built up in a very systematic manner, using the chance in developing a new system based on experience with existing ones. It is divided into General statements, and those for Prevention, Response, Storage and Disposal. Examples are Prevention: P262 = Do not get in eyes, skin, or clothing. Response: P 301+P310 = IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician. P305+P351 = IF IN EYES: Rinse cautiously with water for several minutes.

The GHS labeling system is a transparent, globally harmonised and easily comprehensible hazard communication system, and thus giving the chance for better safety in handling and using hazardous chemicals on a worldwide scale. This new system has to be understood, applied and complied with according to conditions, possibilities and needs of the different target audiences.
EXPOSURE TO ETHYL METHANE SULFONATE IN A PHARMACEUTICAL: RISK ASSESSMENT FOR PATIENTS AND WORKERS


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In 2007, Roche had to recall its anti-HIV drug Viracept (Nelfinavir mesylate) because it was contaminated with amounts of Ethyl Methane Sulfonate (EMS, Ethylmesylate) that exceeded the strict product specifications. EMS was at that time considered a classic non-threshold mutagen that enjoyed a certain popularity as a positive control in genotoxicity assays.

As is the case with many long established chemical entities, the toxicological data base for EMS was found to be restricted to high and toxic dose levels in the pertinent tests and insufficient to conduct a proper ‘low-dose’ risk assessment for the patients who had been exposed to contaminated lots of the drug before the recall. A battery of new tests showed that the mutagenic action of EMS had a clear threshold, thus allowing the calculation of a safe daily exposure of the patient. The results of the key studies and the risk assessment will be presented. Fortunately, the critical dose had not been exceeded by any of the patients and there had been no risk to the health of those who had consumed the drug. The sources of the contamination were eliminated and drug was available again on the market 4 months after its recall.

A risk assessment was also conducted to judge possible risks to the workers who had handled the contaminated material during its manufacture. As expected, worker exposures had also remained below critical levels, but the safety margin was lower than expected. This study will also be explained.

The toxicological investigations of this incident may give rise to the hypothesis that it might be time to question the existence of non-threshold mutagens altogether.
WORKING ENVIRONMENT CONTROL OVER LEAD TOXICITY AT CERAMICS POWDERDUST MANUFACTURING FACTORY

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In medical check-up specialized for workers exposed to lead monoxide powderdust, 7 workers were screened out by the result of high level of blood lead. To measure a working environment at ceramics powderdust manufacturing factory, fourteen sampling points were designed and airborne concentration was analyzed by using Atomic Absorption Spectrometry.

A sampling showed that the value of geometric mean was 0.059 and the value of geometric standard deviation was 3.71. B sampling showed that the value of administrative level was 0.590 (mg/m3). The control class (I) was determined by the calculated value of administrative levels.

Regardless of the high concentration of blood-lead, the control class was not severe.

On the other hand, the concentration of blood-lead (μg/dl), urinary δ-aminolevulinic acid (mg/l), and blood-protoporphyrin (μg/100ml) were monitored in 43 sampling results.

The relationship between blood-lead:x and urinary δ-aminolevulinic acid:y showed co-relative linearity following an equation: y=0.11x-0.61 (P=0.001).

The relationship between blood-lead:x and blood-protoporphyrin:y showed co-relative linearity following an equation: y=4.75x-43.25 (P<0.001).

The relationship between blood-protoporphyrin:x and urinary δ-aminolevulinic acid:y showed co-relative linearity following an equation: y=0.01x+1.67 (P=0.037).

In summary, working environment control is on the assumption of the fixed-location monitoring. However, in real practice, workers never stay still on the spot during their operation. When industrial hygienists assess a working environment, they should be aware that the blood concentration does not always reflect the control class of working environment.
NOVEL APPROACH FOR THE BIOMONITORING OF OCCUPATIONAL EXPOSURE TO 2-CHLOROPRENE

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2-Chloroprene is a high production volume chemical, which is produced in quantities of more than 300,000 tons per year. It is mainly used as monomer for the production of polychloroprene (brand names: Neoprene®, Baypren®). Occupational exposure to 2-chloroprene may occur in its production as well as during the application of the monomer. Because 2-chloroprene is classified as possibly carcinogenic to humans (IARC, Group 2B) an effective tool for the monitoring of the individual exposure to 2-chloroprene is required.

We developed a biological monitoring strategy on the basis of the urinary excretion of several mercapturic acids (MAs) which potentially may derive from the conjugation of 2-chloroprene and its metabolites to glutathione. The selected biomarkers were 4-hydroxy-3-oxo-butyl-MA (HOBMA), 4-chloro-3-oxo-butyl-MA (Cl-MA I), 4-chloro-3-hydroxybutyl-MA (Cl-MA II), 3-chloro-2-hydroxy-3-buteryl-MA (Cl-MA III) and 3,4-dihydroxybutyl-MA (DHBMA). For the quantitative determination of MAs we applied an online extraction and enrichment step with a subsequent analytical separation by high performance liquid chromatography and detection by tandem mass spectrometry. The detection limits ranged from 2.4 (Cl-MA III) to 8.2 µg/l (DHBMA). The method was applied to urine samples of 14 employees occupationally exposed to 2-chloroprene and of 30 subjects without any occupational exposure to 2-chloroprene.

Cl-MA I and Cl-MA II were not detected in any of the samples. In the urine samples of the control group Cl-MA III was also not detectable, whereas we detected this metabolite in 11 urine samples of the exposed group (median 6.1 µg/g creatinine, max 25.7 µg/g creatinine). Furthermore, we discovered significantly elevated urinary levels of DHBMA (medians 3,255 vs. 179 µg/g creatinine) in occupationally exposed workers. HOBMA was also detected in each urine sample of the exposed group (median 214 µg/g, range 98 - 436 µg/g). However this levels were not statistically different from the background values in the control group.

The mercapturic acids DHBMA and Cl-MA III seems to be suitable biomarkers for occupational exposures to 2-chloroprene. DHBMA occurs as main product in 2-chloroprene metabolism and as most sensitive parameter. The determination of Cl-MA III in urine becomes important in cases of coexposure to 1,3-butadiene, because DHBMA do not distinguish between 1,3-butadiene and chloroprene exposure.
THE USE OF BIOLOGICAL REFERENCE VALUES FOR THE EXPOSURE ASSESSMENT OF CHEMICAL SUBSTANCES AT THE WORKPLACE

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In general, health based biological exposure limits are established for biological monitoring in the prevention of occupational diseases. However, this approach is not feasible for chemicals with the ability to produce adverse effects without threshold concentrations, e.g. genotoxic carcinogens. An assessment of the exposure to these chemicals may be achieved by the comparison to safety values based on best practice, cancer risk and background exposure, respectively. For the latter approach the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area of the Deutsche Forschungsgemeinschaft (DFG MAK commission) evaluates biological reference values for chemical compounds at the workplace, which are titled “Biologische Arbeitsstoff-Referenzwerte” (BAR). This contribution provides an introduction of the BAR approach and presents the status quo of BAR values.

BAR relate to background levels of substances present in biological materials in a reference population of persons of working age who are not additionally occupationally exposed to the substances. BAR values are derived from the 95th percentile of biomarker levels in random samples from defined population groups. The DFG MAK commission advises that the background levels can be influenced by such factors as age, sex, social status, residential environment and lifestyle. The DFG MAK commission publishes BAR documentations in German and in English.

Since 2008, BAR have been established for 14 chemical compounds or groups of chemicals: Acrylonitrile, 4-Aminobiphenyl, Arsenic and inorganic arsenic compounds, Barium compounds, Beryllium and its inorganic compounds, Cadmium and its inorganic compounds, Chromium and its inorganic compounds, 4,4’-Diaminodiphenylmethane, Manganese and its inorganic compounds, Nickel and its compounds, o-Toluidine, Trichloroethylene, 2,4,6-Trinitrotoluene and Vinyl chloride. In the case of Acrylonitrile, 4-Aminobiphenyl, Cadmium and o-Toluidine the BAR were based only on data from non-smoking populations due to a distinct influence of smoking habits on the biomarker levels.

The BAR approach of the DFG MAK commission allows the identification of additional occupational exposure to hazardous substances by comparison of biomonitoring results with the general background levels. An exceeding of a BAR value does not indicate an unacceptable health risk; however the BAR may be used as goal-setting in the improvement of occupational hygiene.
THE CONCEPT OF SCOEL TO SET OELS

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The Scientific Committee on Occupational Exposure Limit Values (SCOEL) advises the European Commission on occupational exposure limits for chemicals in the workplace. SCOEL is composed of 21 members selected from candidates proposed by the EU Member States and appointed by the Commission. They are experts in chemistry, toxicology, epidemiology, occupational medicine or industrial hygiene and act as independent scientific experts.

The "Methodology for the Derivation of Occupational Exposure Limits: Key Documentation" (December 2009) describes the general principles of the case by case evaluation of chemicals to define the eight hour time weighted average (TWA) exposure limits, the short term exposure Limits (STELs), health based biological limit values (BLVs), application of uncertainty factors, and consideration of reproductive toxicity for identification of the TLV, labelling respiratory sensitizers, and skin notation.

Chemical carcinogens and mutagens are evaluated as follows:
Group A: Non-threshold genotoxic carcinogens; for risk low-dose assessment the linear non-threshold (LNT) model is applicable.
Group B: Genotoxic carcinogens, for which the existence of a threshold cannot be sufficiently supported. The LNT model may be used as a default assumption.
Group C: Genotoxic carcinogens for which a practical threshold is supported.
Group D: Non-genotoxic carcinogens and non DNA-reactive carcinogens with a true ("perfect") threshold, which is founded by a NOAEL.

Health-based OELs are derived by SCOEL for carcinogens of groups C and D.

Based on the available scientific information draft recommendations are prepared by individual members and after approval during one of the 4 annual SCOEL meetings undergo a stakeholder consultation to allow interested parties to submit scientific comments and further data.

So far, 161 summary documents (SUMs) have been completed, 12 are on going and 7 are planned.
On April 25, 2006 various trade unions and employers’ representatives signed the first European multisector agreement to protect workers from health risks associated with exposure to respirable crystalline silica dust. It covers more than two million workers in 15 different sectors in every EC member state. Put into force on October 26, 2006 the agreement aims to reduce worker’s exposure to respirable dust in the long term through good practice in the workplace.

The basic element of the agreement is the Good Practice Guide providing guidance to risk assessment for silica exposure. It includes also a collection of task sheets describing tailor-made safety measures for specific working operations to minimize the exposure effectively. The Good Practice Guide serves as a tool to implement standardised protective measures and to provide information, training and health surveillance to the workers.

The implementation and sustainability of the process is being monitored by a biennial reporting scheme providing data on key indicators that allow the signatories and also the European Commission to assess the progress and improvement of the situation in the companies.

The results and experiences gained by implementation and reporting and the significance and usability for similar projects in occupational health and safety will be discussed.
EVALUATION OF WORK-RELATED PSYCHOSOCIAL AND ERGONOMICS FACTORS IN RELATION TO LOW BACK DISCOMFORT IN EMERGENCY UNIT NURSES

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BACKGROUND AND AIM: Nursing is categorized in occupations with high prevalence of low back pain. The aim of this study was to evaluate the relation of intensity of low back discomfort with two factors that contribute to low back pain -Ergonomics risk factors and psychosocial factors- most seen in emergency unit nurses.

MATERIALS AND METHODS: This cross-sectional survey was conducted on 120 emergency unit nurses in Isfahan. For daily assessment of psychosocial and Ergonomics factors and intensity of Low back discomfort, questionnaires such as: Job Content, Ergonomics hazards and Nordic questionnaire were used respectively. Nurses were questioned during a 5-week period, at the end of each shift work. Using Spearman, Mann-Whitney and Kolmogorov-Smirnove test, the final results were analyzed with SPSS software18/PASW.

RESULTS: There was significant relationship between work demand, job content, social support and intensity of low back discomfort (P-value<0.05). But there was not any link between intensity of Low Back discomfort and job control. Also there was significant relationship between Intensity of low back discomfort and Ergonomics risk factors.

CONCLUSION: This study showed that intensity of low back discomfort will increase with decreasing social support and increasing work demand, Job Content, Ergonomics factors (Awkward Postures (rotating and bending), manual patient handling and repetitiveness, standing continuously more than 30 minutes). So, to decrease work related low back discomfort, psychosocial factors should be attended in addition to Ergonomics factors.

KEY WORDS: Work-related psychosocial factors, Ergonomics factors, Low back pain, Emergency unit.
STUDY OF ASSOCIATION BETWEEN JOB STRESS (BASED ON JOB DEMANDS AND CONTROL MODEL) AND CARDIOVASCULAR DISEASE RISK FACTORS AMONG PETROCHEMICAL COMPANY PERSONELL

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BACKGROUND, OBJECTIVES: The combination of high psychological job demands and low decision latitude (high job strain) has been associated with an increased cardiovascular risk factors. This study was the first one which has used job demands and low decision model (jd & c) to measure job stress in an Iranian group of workers to assess adverse effects of job stress on cardiovascular risk factors. The aim of this study was to examine relationship between job stress and cardiovascular risk factors including high blood pressure, BMI, cholesterol, smoking status, heart rate.

METHODS: This cohort study was conducted among 500 randomly selected employees of petrochemical company. two self-administrated questionnaires included job demands and control and job stress in formation were used to collect data. individuals demographic data and cardiovascular risk factors were collected from health records.

FINDINGS: There was a significant relationship between job demands and decision latitude ($\chi^2=28.295$, sig=0.000). There was also a significant relationship between job demands and decision latitude and stress (low stress: $\chi^2=15.154$, sig=0.000, moderate: $\chi^2=9.642$, sig=0.047 and relatively high: $\chi^2=26.321$, sig=0.004). A significant relationship has been seen between job stress and age ($\chi^2=30.941$, sig=0.000); job grades: (sig=0.000, $\chi^2=70.702$), education: ($\chi^2=58.737$, sig=0.000), and marital status: ($\chi^2=24.801$, sig=0.001). According to JD&C model, workers with stress have shown an excess risk of (sistol, $\eta=0.684$- diastole: $\eta=0.696$) for hypertension ($\chi^2=35.652$, sig=0.000), for being smoker ($\chi^2=38.371$, sig=0.000), for BMI ($\eta=0.469$ for high cholesterol), and finally ($\chi^2=145.078$, sig=0.000) for heart rate.

CONCLUSION: This prospective cohort study showed an increase in cardiovascular risk factors by increasing in job stress. It is recommended to use this model to examine effects of job stress on cardiovascular system among women and other industries as well.
THE ROLE OF EXPERT JUDGEMENT AND CONCEPTIONAL APPROACHES IN SETTING OELs BY THE GERMAN MAK COMMISSION

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The “DFG Commission for the Investigation of Health Hazards of chemical compounds in the Work Area” (“MAK Commission”) is a scientific commission dealing with manifold aspects of evaluation and classification of hazardous substances at the work place. One main activity consists in the establishment of MAK and BAT values. They are based on available data with respect to epidemiological findings, occupational medical reports, toxicological properties as well as mechanistic data concerning the mode of action. For substances without genotoxic and/or carcinogenic properties, MAK and BAT values are derived from the “no observed adverse effect level” (NOAEL) of the most sensitive endpoint of toxicological concern, taking into account local and systemic affects. In case of missing crucial information, substances are listed in group IIb and no value will be stated. Furthermore, occupationally relevant substances are evaluated with respect to carcinogenic, germ cell mutagenic and sensitizing properties as well as percutaneous absorption and potential reproductive toxicity and classified accordingly. Within these evaluations, conceptional work is of increasing importance. For example, carcinogenic substances are grouped in one of five categories, based on epidemiological evidence, animal data and mechanistic information on the mode of action, considering also the potential risk at exposure conditions on which the MAK values are observed. Other examples for conceptional work are the evaluation of granular biopersistent dust, of fibers, of metals and their compounds and of nanomaterials; here, specialized expert working groups within the MAK commission discuss, based on scientific evidence, potential grouping of substances with respect to setting of exposure limits, classifications and/or research requirements. In all cases, available data are checked for validity of the respective studies and evaluated on a case-by-case basis. Extrapolation from animal data and the establishment of the margin between between NOAEL and MAK/BAT values is done by expert judgement, not by general extrapolation factors. Consideration will be also given to the analytical surveillance of MAK and BAT values, accompanied by the development of methods for analysis in air and biological materials. Exposure limits, notations and classifications are published annually in the List of MAK and BAT values. Furthermore, a detailed scientific documentation of each decision is published in the „Toxikologisch-arbeitsmedizinische Begründungen“, available also in an English translation.
EVALUATION OF NANOPARTICLES BY THE GERMAN MAK COMMISSION: CURRENT STATUS AND RESEARCH NEEDS

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Nanomaterials are widely distributed in the environment and at workplaces. Nevertheless, the issue of risk assessment appears to be far behind the growing field of applications and is yet important to support the manifold potentials of nanotechnology. Even though there have been increasing numbers of publications related to the potential toxicity of nanomaterials, the interpretation of the results is often limited due for example to insufficient characterization of the particles under investigation. Aim of the MAK working group is to summarize current scientific evidence required for risk assessment of nanomaterials with respect to workplace exposure. Within this task, the principal question to be answered is whether or not there are modes of action and/or target organs unique for nanomaterials as compared to particles in the microscale range. Since the goal is risk assessment and not only hazard identification, emphasis is given on available data allowing the establishment of dose-response relationships with respect to exposure and biological effects, i.e. toxicokinetic and toxicodynamic interactions. At present, only few quantitative data from in vivo studies are available; therefore, it is important to set up test strategies for both in vitro and in vivo testing to identify general criteria for grouping of nanomaterials and subsequent risk assessment. For example, one question concerns the comparison of nanoscale and microscale biopersistent particles of the same material considering systemic bioavailability, target organs and the identification of critical reactions, including indirect/direct genotoxicity. With respect to metal-based particles, differences in the uptake and intracellular release of metal ions appear to be relevant. Also, coated materials should be evaluated with regard to the intracellular deliberation of potentially toxic compounds such as metal ions from “quantum dots”. Finally, nanotubes should be assessed in comparison to fibres of microscale dimensions. Altogether, to achieve relevant information for risk assessment, comprehensive particle characterization as well as dose-response-studies with respect to all relevant endpoints under investigation are highly required.
Airborne nanotechnological products in a size ranging from 1 to 100 nm do have chemical and physical properties that in most instances are quite different from larger-sized bulk material. In contrast to particle number and surface, mass and volume no longer matter in this nanosize range. For this reason, there is the assumption that - compared to larger-sized material - nanomaterial may interact differently with cellular and subcellular structures. Does this assumption correspond to the findings and what is the evidence for the results that 0.01 and 0.1 µm particles may elicit not only quantitatively but also qualitatively different biological responses compared to, as for instance, 1 µm particles?

For airborne particles the respiratory tract and the lung are the primary target organs. Particle deposition in the lung and alveolar particle clearance are species-specific processes leading to different local particle doses and by this to various particle-related responses in different animal species and in humans exposed to the same particle concentration. The specific effects of a particle are determined by its solubility / biopersistence, surface characteristics, crystallinity and chemical composition.
The toxicological health risk assessment of mercury (Hg) was conducted on an oil and gas personnel and contractors who were involved in 13 major and minor shutdowns at 3 platforms. Based on the availability of data on various parameters including biological monitoring, ambient and personal air monitoring and dietary mercury level, platform 2 was selected for risk assessment. The methodology for quantitative risk assessment was carried out according to the WHO Human Health Risk Assessment Tool Kit. All databases related to Hg activities between 2006-2010 were utilized for analysis of potential sources of exposure through air, water and food. Furthermore, the levels of Hg in condensate, crude oil, food from the galley and in personnel's blood and urine were investigated. The species of Hg present in the condensate and crude oil was primarily elemental but organic Hg was predominantly found to be present in fish at the galley. Hg was not detected in the water and this route of exposure is not significant for the purpose of risk assessment. Preshift and postshift blood data from 2671 and 2502 personnel respectively were analyzed for Hg potential exposure. From the preshift total blood Hg, only 78 (2.9%) personnel had Hg level exceeding the Biological Exposure Index (BEI) confirming that the high exposure was unrelated to the workplace but potentially due to dietary intake especially seafood or other sources. In the postshift blood Hg analysis, 94 (3.8%) personnel showed blood Hg above BEI. Following a review of the investigation report, ambient and personnel air monitoring data and blood speciation results, only 13 (0.52%) personnel were confirmed to experience occupational exposure to Hg during the shutdown activities. The small percentage of confirmed occupationally exposed personnel from all the shutdowns demonstrates an effective implementation of the company’s mercury control measures. In contrast, the remaining 81 (3.2%) personnel had Hg exceeding BEI most probably due to ingestion of Hg from the seafood in the galley. Health risk assessment calculation indicates that those personnel categorized as high fish intake group are at risk of exceeding the acceptable daily intake of Hg. However this is a public health issue and since the dietary habit is a personal choice, the management can only inform the personnel of the risks of high fish intake. Taken together, the results of this risk assessment and the nature of exposure to elemental and inorganic mercury in crude oil and condensate, urine Hg corrected to creatinine level is a better occupational exposure biomarker for the company’s personnel since total blood Hg may also reflect exposure from dietary intake.
MYCOTOXIN SCREENING METHOD USING A MTT CLEAVAGE ASSAY FOR ENVIRONMENTAL AND OCCUPATIONAL HEALTH STUDIES

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In environmental and occupational studies of bioaerosols the risk assessment is typically based solely on fungal identification and quantification, but appears often poorly correlated with specific epidemiological health outcomes. This may be due to biological fungal air contaminants that have different toxic properties. Traditional in-vitro chemical laboratory analysis of fungi have practical limitations. In-vivo toxicity screening test appear preferential to explore complex health reactions reported by exposed patients, particularly unusual immunological and neurological abnormalities.

In this field study, we compared conventional fungal identification methods with a newer screening test for mycotoxins (cytotoxicity of mycotoxins evaluated by the MTT-cell culture assay) and EIA quantification of trichothecenes designed for detection of Roridin A and other macrocyclic trichothecenes. High (24h) volume air sampling to collect airborne particles (n=210) was conducted in homes and work places of patients (n=100) with environmental symptomatology and visible fungal indoor growth. The crude extracts of approximately two third of the air samples showed mild to high (+ to ++++) toxicity in the MTT cytotoxicity assay and 19 % of n=176 samples had Roridin A results of >10 ng/g. Among all the fungi identified, there was only a weak association of viable Stachybotrys fungi and Roridin A (Spearman rank order, p=0.009), but not with other fungi. In conclusion, traditional fungal identification methods in bioaerosols exposure studies appear to be limited and a poor predictor of (trichothecene) toxicity without the results and use of the effect based toxicity bioassay to assess and confirm toxicity.

The MTT cell culture cleavage assay is an effect based screening test which has been found to be quick and easy to perform evaluations of the biological activity of many different mycotoxins and may also provide a useful tool for the testing of a large variety of sample materials, including indoor air contaminants.
Physiologically Based ToxicoKinetic (PBTK) models can predict the level of a chemical in body tissues and body fluids following inhalation and/or dermal exposure. However, PBTK-models generally have the drawback that a large number of substance-specific partition parameters need to be defined for a simulation. A newly developed generic PBTK-model, called Indus-ChemFate, contains algorithms as QSPRs (Quantitative Structure Property Relationships) to estimate the partitioning in the body. This QSPRs for blood:air and tissue:blood partitioning are based on the physical-chemical properties: octanol/water partition (log Kow), molecular weight (MW), density, vapor pressure and water solubility. Thus, the generic PBPK model can be used for simulations of multiple data-poor chemicals. The model is programmed as a macro in Visual Basic and it runs in Microsoft Excel.

The IndusChemFate PBTK-model assumes a 70 kg reference human and considers three routes of exposure (inhalation, dermal and/or oral). All physiological parameters are adopted from reference documents. The model has two built-in exercise levels. A few physical-chemical properties and metabolism kinetics of the chemical of interest are required as input data to run the model. Dermal uptake is simulated for vapor and liquid skin contact. Dermal uptake by direct skin contact with liquids assumes deposition over an assigned exposure period, for instance a 8-h working day. Key feature of this module is that evaporation (from applied dermal dose and from stratum corneum) is fully accounted for. Oral intake of compounds is modelled as a bolus dose that is directly applied to the stomach. Michaelis-Menten saturable metabolism is incorporated in the liver. Metabolism can also be modeled in 10 other organs/tissues. Up to 4 subsequent metabolites can be simulated. Entero-hepatic circulation of phase II metabolites is optional at a user-defined rate.

A number of published studies of inhalatory and/or dermal exposure was used to compare the measured concentrations in blood and urine with the predicted concentrations by the IndusChemFate model. Comparisons of model-simulations with data of published studies of exposed volunteers and/or workers will be shown for PAH-exposure and urinary 1-hydroxypyrene-glucuronide excretion, after inhalation and dermal exposure. But also for MTBE inhalation and urinary MTBE-metabolites, for heptane inhalation and the metabolites 2-heptanol and 2-heptanone in blood and for ethanol consumption and ethanol concentration in expired air. Real-time simulations will be demonstrated to get an impression of the transparency of the results of predictive simulations. Model outcomes have an accuracy within an order of magnitude. The model IndusChemFate should be regarded as a first tier tool or screening tool for data-poor compounds.

The software is available as freeware. The program and user manual are downloadable from the site: www.cefic-lri.org/lri-toolbox/induschemfate. The research work has been funded by CEFIC-LRI.
AROMATIC AMINES AND BLADDER CANCER - CURRENT AND FUTURE BIOMARKERS FOR HEALTH PREVENTIVE MEASURES


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Aromatic amines are high production volume chemicals and are mainly used as intermediates in the synthesis of medications, pesticides, colorants, and antioxidants. Exposure to aromatic amines occurs at the workplace and via the environment. Various aromatic amines are known to be mutagenic and carcinogenic, e.g., capable of inducing bladder cancer in humans. Therefore, health preventive measures are of utmost importance in order to reduce exposure and risk to humans.

An overview on the possibilities and limitations of current and future biomarkers for health preventive measures in populations exposed to aromatic amines is presented. Particular focus is on the use of biomarkers of exposure and effect in order to create sound-scientific results for exposure assessment, risk assessment, and risk management. Examples include primary health preventive measures at the workplace and in the environment in order to assess exposure to aromatic amines in humans. For this purpose, biomarkers of internal and effective dose such as aromatic amines in urine and hemoglobin adducts in blood of exposed persons can be used. In addition, examples of secondary health preventive measures for the early detection of bladder cancer in humans are presented. For this purpose, biomarkers of altered structure and function such as chromosomal aberrations, gene and protein expression, and epigenetic alterations are discussed.

In summary, the examples will show that a biomarker-based approach is an essential part of occupational and environmental health surveillance of both, individuals and populations, exposed to aromatic amines. In future, the results of such studies are capable to reveal time trends in exposure, identify persons and populations at risk, foster intervention studies, and validate potential biomarkers for early detection of bladder cancer. Finally, the use of both, biomarkers of exposure and effect, will contribute to sound-scientific decisions on the regulatory level and to risk assessment in terms of unraveling the mosaic between exposure to aromatic amines and onset of bladder cancer in humans.
UNCONVENTIONAL THREATS TO CORPORATE LEADERSHIP:
GENERAL CONCEPTS OF PREPAREDNESS; RECOGNITION AND MITIGATION

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Recently, the term “WMD” which had been commonly thought of as “Weapons of Mass Destruction” was redefined as “Weapons of Mass Disruption”. The driving force in this new WMD definition was the recognition that unconventional attacks, including use of Chemical, Biological, and Radiological (CBR) agents, have significant potential to disrupt the basic functions and infrastructure of society on the same order as a nuclear weapon. A key lesson to take from this shift in thinking is that the users’ goal of disruption is not necessarily to physically destroy large areas or kill large numbers of people, but to fundamentally affect the functioning of the target, thus opening the door for spreading their interests. Large multi-national corporations or even regional companies that have a dominant role in a business sector or a regional economy make excellent targets for a group that wants to cause economic disruption. These types of organizations have long recognized the potential traditional threats to their leadership and applied principles of protective security, but this new WMD threat is typically beyond the experience, training, and expertise of security providers. Unlike traditional ballistic weapons, where an organization’s medical staff could only play a role in addressing the effects of an attack, medical staffs have the basic science background critical to playing an important role in prevention, recognition, and mitigation of an effective CBR assault on their organization. This session will provide medical staff with an overview of the history and capability of unconventional WMD agents against leadership targets and provide a strategy for working with security and protective staff to develop a comprehensive readiness strategy.
BLOOD AHR ACTIVATOR LEVELS AND DISEASE ODDS RATIOS IN POPULATIONS WITH HIGH AND BACKGROUND EXPOSURE TO PCP WASTE

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Residents in an area contaminated by an abandoned PCP manufacturing plant in Southwestern Taiwan have higher PCDD/PCDF levels in serum. These dioxin-like compounds would abnormally raise their xenobiotic receptor (AhR) activity.

A total of 504 subjects, 271 residents of the high exposure area (Annan District, Tainan) and 210 from a non-exposure area serving as reference group were recruited for the study. Volunteer participants with informed consent completed a questionnaire concerning general lifestyle and self-reported diseases. Blood were collected for health check analyses and determination of bioactive dioxin-like compounds with CALUX system (acetone-hexane extracted lipids were clean up with a special column and tested against a mouse hepatoma (Hepa1c1c7)-derived cell line which has been stably transfected with the DRE-driven firefly luciferase reporter plasmid, pGudLuc6.1).

Exposure area residents had relatively higher AhR activator levels than control area residents (average= 144.47 vs. 72.43 pg TEQ/g fat). After controlling for age, BMI, and smoking status, the differences were still statistically significant, either considering both genders together or separately. Logistic analysis of disease odds ratios with age, BMI and smoking status adjustment showed that people with higher AhR activator levels (> 99.5 pg TEQ/g fat) had higher risk for cancers (OR=4.876, 95%CI=1.119-21.231). Disease odds ratios for residents from the exposure area was higher for hepatitis B (OR=4.855, 95%CI=1.862-11.309), general pain (OR=2.845, 95%CI=1.597-5.069), sciatic pain (OR=2.102, 95%CI=1.032-4.282) and migraine (OR=1.710, 95%CI=1.120-2.609).
CROSS-SECTIONAL AND LONGITUDINAL STUDIES OF HEALTH EFFECT MARKERS AMONG ENGINEERED NANOMATERIAL EXPOSED WORKERS

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OBJECTIVE: The aim of this study is to establish and to identify the health effect markers on workers with potential exposure to nanoparticles during manufacturing and/or application of nanomaterials.

METHODS: We recruited 227 nanoparticle-exposed workers and 137 non-exposed workers from 14 plants in Taiwan. Questionnaire was used to collect exposure status, personal data and potential confounders. The health effect markers investigated cross-sectionally and longitudinally include pulmonary and cardiovascular disease markers, inflammation markers, oxidative stress markers, antioxidant enzymes, and genotoxic markers. Control banding from Nanotool Risk Level Matrix was adopted to categorize the exposure levels (RL 1 to RL 4).

RESULTS: Significant depression of antioxidant enzymes (superoxide dismutase (SOD) and glutathione peroxidase (GPX)) and Significant increase of cardiovascular markers (fibrinogen, ICAM, and IL-6) were found cross-sectionally in potentially nanoparticle-exposed workers. Correct rate of 7-digit reverse memory was significantly lower in exposed workers than in controls and a significant reversed gradient was also found for correct rate of memory (p<0.05 for test for trend). Similar to the findings from cross-sectional study, depression of antioxidant enzymes (SOD, GPX) and change of cardiovascular markers (increase of VCAM and decrease of paroxonase) were significantly associated with nanomaterials handling in half a year follow-up. In addition, small airway damage marker (CC16) and lung function were also associated with nanomaterials handling in this half a year follow-up study. The change of inflammation markers (increase of NFkB), cardiovascular markers (increase of IL6sR, decrease of arylesterase), and genotoxic markers (increase of %DNA in tail and olive moment) were significantly associated with exposure during the one and a half years follow-up.

CONCLUSIONS: Depression of antioxidant enzymes and increase of cardiovascular markers were found in potentially nanoparticle-exposed workers. Biomarkers of antioxidant enzymes, such as SOD and GPX and cardiovascular markers, such as fibrinogen, ICAM or VCAM, IL-6 or IL-6sR, paroxonase or arylesterase can be served as biomarkers in medical surveillance of engineered nanomaterial handling workers.
SHIFT WORK AND CANCER – STATE OF SCIENCE AND PRACTICAL CONSEQUENCES

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Nearly 20% of the working population in Europe and North America is engaged in shiftwork, and - owing to the nature of the production processes involved - the chemical industry is particularly dependent on this type of work organization. In December 2007, an expert Working Group convened by the IARC Monographs programme has concluded on the basis of “limited evidence in humans for the carcinogenicity of shift-work that involves nightwork”, and “sufficient evidence in experimental animals for the carcinogenicity of light during the daily dark period (biological night)” that shift work that involves circadian disruption is probably carcinogenic to humans (Group 2A).

WHICH NEW INSIGHTS HAVE EMERGED IN THE MEANTIME? Since the IARC assessment, several new studies have been published, with inconclusive results. Heterogeneity of study exposures and outcomes and emphasis on positive but non-significant results make it difficult to draw general conclusions. Further data are needed for additional disease endpoints and study populations. Also, several reviews and commentaries, which have been published meanwhile, came to equivocal results. Published evidence is widely seen as suggestive but not conclusive for an adverse association between night work and breast cancer, and limited and inconsistent for cancers at other sites and all cancers combined.

THE BASF SHIFT WORK SYSTEM: It is quite obvious that due to technical, cultural and economic reasons shift work cannot simply be avoided in a modern society. In the face of a possible health threat and the absence of certainty, non-action is nevertheless not an option. In a previous study we observed neither an elevated risk of total mortality nor an cancers increased incidence, albeit on an incomplete database, in a cohort of more than 13,000 BASF shift workers compared to 17,000 day workers, followed up until the end of 2006. An additional analysis targeted on cancer mortality between 2000 and 2010 also failed to produce indications of an elevated cancer risk associated with shift work. The peculiarities of the BASF shift system, which may contribute to these “non-effects”, will be discussed.

CONCLUSION: We concluded that, even if the purported association was true, the BASF shift system appears not to be prone to causing circadian disruption.
OCCUPATIONAL HEALTH DURING THE DECOMMISSIONING OF MERCURY CELLS PLANTS

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Since the end of the 19th century, the mercury process has been used in chlorine production. This process requires a large amount of mercury, about 400 tons for a chlorine capacity of 150 000 tons per year.

In spite of all the precautions, some mercury is released in the environment, essentially in liquid effluent streams. Euro Chlor, representing the European chlorine industry, has committed that the electrolyses using mercury cell technology should be shut down before 2020 and the equipments demolished.

Recommendations regarding occupational health and industrial hygiene in actively producing plants have been published previously. In the meantime, several mercury cell rooms have been shut down. The European chlorine producers have pooled their experience in order to define the best available technique for the decommissioning during the coming decade. This presentation contains guidelines for workers’ health protection specifically during the decommissioning of mercury electrolyses.

Mercury exposure is much higher during decommissioning than during the operation period. The first reason is the mobilisation of mercury that has migrated in materials, such as cements or metals. The second reason is the mobilisation of mercury deposited on girders, beams and so on, over decades of operation.

The kinetic of exposure is also different. During regular production it is rather stable. During decommissioning, there are short periods of high exposure and a very large variability from one day to another. The resulting difficulties for risk management will be illustrated by examples.

So, we will point out the specific aspects of occupational health and industrial hygiene regarding mercury during decommissioning.
OTOTOXIC SUBSTANCES AT THE WORKPLACE

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The European Noise Directive 2003/10/EC stipulates that “the employer shall give particular attention, when carrying out the risk assessment, to […] any effects on workers’ health and safety resulting from interactions between noise and work-related ototoxic substances”.

Ototoxic chemicals cause reversible or irreversible effects that impair the senses of hearing or balance. These can be induced by disturbing the structures and/or the function of the inner ear (auditory and vestibular apparatus) and/or the connected neural pathways from the inner ear up to (and including) the auditory cortex in the brain.

Comprehensive literature reviews have recently been published by the Canadian Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST, 2009) and the European Agency for Safety and Health at Work (2009), as has a joint evaluation by the U.S. National Institute for Occupational Safety and Health (NIOSH) and the Nordic Expert Group (2010).

The presentation addresses the relevant results of the three approaches and draws general conclusions for occupational hygiene. This includes the identification of critical workplace substances, considerations regarding the effect in combination with noise and a comment on the call for lowering of the established occupational exposure limits owing to ototoxic effects.
Exposures of humans to nano-sized particles has occurred throughout human history, and it is only with the more recent advent of nanotechnology and its application for diverse industrial, medical and consumer uses that reports about the potential of engineered nanomaterials causing adverse health effects has raised serious concerns. Such concerns stimulated research in a still emerging field of nanotoxicology, resulting in a steadily increasing number of publications showing that engineered nanomaterials – because of their specific physico-chemical properties – can induce significant adverse effects. Although most of these studies were performed using unrealistic exposure scenarios, they have led to a widespread perception that essentially all nanomaterials are “toxic” and pose a significant health risk. Knowledge about potential human and environmental exposure combined with dose-response toxicity information will be necessary to differentiate real from perceived risks of nanomaterials following inhalation, oral or dermal routes of exposure. The respiratory tract is the major portal of entry for airborne nanoparticles; using this exposure route as an example, some key concepts of nanotoxicology will be discussed, including the significance of dose, dose rate, dosemetric, and biokinetics. The importance of characterizing critical physico-chemical properties of nanoparticles is emphasized, specifically surface properties that influence their biological/toxicological properties, cell-interactions and biokinetics. Thus, for example, the appropriateness of altering nanoparticle surface characteristics via use of dispersants or by harsh sonication procedures in preparation for toxicity testing needs to be critically evaluated. Misconceptions need to be corrected, such as the propensity of nanoparticles to translocate with high efficiency across barriers, or that the identification of a hazard based on unrealistic and unjustifiable high dose studies represents a useful basis for risk assessment. On the other hand, study results based on improbable high doses, in vitro as well as in vivo, may be viewed as proof-of-principle studies to be validated by appropriately designed follow-up studies using justifiable relevant exposures. Under such realistic conditions, many engineered nanoparticles may be unlikely to induce adverse effects, although still largely unknown are effects of chronic, low level exposures. Validation of in vitro results by in vivo studies is essential and should be based on dosimetric and biokinetic information; extrapolation from animal studies to humans requires careful analysis and interpretation of dose-response data. Without being able to perform an appropriate risk assessment for a specific nanomaterial, it is prudent to prevent exposures by precautionary measures/regulations.
A NEW METHOD OF MISBALANCE CORRECTION OF ECOLOGICALLY ME-
DIATED SYNDROME OF INCREASED CHEMICAL SENSITIVITY IN CHILDREN AND
JUVENILES

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Nowadays the tendency of trace elements imbalance development in children with elev-
ation of toxic elements has been noted in Belarus.

New method of correction including urine excretion level determination of lead, zinc, cooper was developed in order to increase the treatment efficiency of circumscribed alopecia caused by dysmicroelementosis in children and adolescents. The patient was prescribed Kyolic 1 capsule 0,7 gr 3 times a day; Spirulina platensis 1-2 tablets 0,4 gr 3 times a day and Sophora japonica decoction 1 teaspoonful 3 times a day simultaneously during two months in case of lead level increase from 0,1 mg/l to 0,2 mg/l cooper and zinc level increase in case of alopecia foci appearance not longer than 2 months ago. The objective of the present study was to correct nutritional pattern in children with the syndrome of the chemical hypersensitivity.

The new method was applied in 32 patients children and juveniles living in Belarus and Russia, aged from 4 to 17 years, with the clinical manifestations of alopecia areata. 18-control group 29 patients demonstrated complete hair growth regeneration while a positive outcome of body detoxification was marked. It was proved by microelement urine composition before and after complex treatment.
UROSCREEN – TUMOR MARKERS FOR EARLY DETECTION OF BLADDER CANCER IN CHEMICAL WORKERS


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OBJECTIVE. To assess the performance of tumor markers in bladder cancer screening in a prospective study.

SUBJECTS AND METHODS: From September 2003 to January 2010, 1610 men took part in an annual voluntary bladder cancer screening program for chemical workers with former exposure to aromatic amines. A total of 7,219 urine samples was collected for early detection of bladder cancer using cytology, NMP22, and UroVysion test. Survivin was investigated as a not yet approved marker. Hematuria and urinary leukocytes were determined with dipsticks followed by a sediment analysis. Potential predictors of positive test results were estimated using a generalized estimating equation model for repeated urinalysis. The bladder cancer risks were estimated for the highest value of a tumor marker during the study with Poisson regression.

RESULTS: As of December 2010, 20 bladder tumors were detected in 19 participants. This low incidence resulted in low positive predictive values (PPVs) of all tumor tests. However, the marker panel detected at least 15 cases depending on the cut-off for a positive test result. Reasons for false-negative cases were also a low compliance for annual screens and limited urine quality. Urinary leukocytes were associated with positivity of both NMP22 and Survivin whereas cell-based test were not affected by hematuria or leukocytes.

CONCLUSIONS: The low bladder cancer incidence resulted in low PPVs of all tumor tests. However, the marker panel performed well in the detection of bladder cancer at early stages. NMP22 resulted in a larger fraction of false-positive results than the other tests due to a variety of confounding factors.
The investigation aimed at assessing exposure levels of metals in general environment and imminent risks of adverse effects in women of reproductive age and in the newborn due to prenatal exposure. The study included 406 healthy women who gave vaginal birth at term in a clinical hospital in Zagreb, Croatia. We measured concentrations of toxic metals cadmium, lead, and mercury, and of essential micronutrients iron, zinc, copper, and selenium in samples of maternal venous blood, umbilical cord blood, and placental tissue (using standard analytical techniques, AAS and ICP-MS). We also assayed steroid hormones in placental tissue ex vivo (using enzyme-immunometric method). All data were statistically analysed in relation to the most common sources of metal exposure, which are food and cigarette smoking. None of the subjects was occupationally exposed to either metal.

In maternal blood of smokers, cadmium was as twice as high as in non-smokers and correlated with smoking habit in pregnancy. In cord blood of smoking mothers, cadmium was ten times lower than in maternal blood and did not differ from non-smoking mothers. There were no differences in blood lead or in serum iron, zinc, copper, and selenium concentrations between smokers and non-smokers. Mercury in maternal and cord blood and selenium in maternal and cord serum increased linearly with dietary intake of fish.

In smokers, placental cadmium was twice as high as in non-smokers, placental lead was higher, while birth weight, birth length, and birth weight/placental weight ratio were lower than in non-smokers. The levels of both toxic metals inversely correlated with birth weight. Placental zinc was higher in smoking mothers (making it less available to the foetus), and iron and copper did not change. Progesterone and estradiol levels in placental tissue correlated, and we found no significant difference between smoking and non-smoking mothers (in a preliminary study, we observed lower placental progesterone in smokers; Piasek et al., Reprod Toxicol 2001;15:673-681).

This study confirms that, beside blood and serum, human placenta can make a unique and useful tool for biological monitoring of metals from external maternal environment and, at the same time, within the maternal organism that is internal environment for foetal development. Exposure to toxic metals in the women of Zagreb County is similar to other continental big European city areas, and does not pose a serious threat for the unborn child. Exposure to tobacco smoke, due to cadmium bioaccumulation and action in placental tissue, may adversely affect placental function in transport of essential micronutrients to the foetus (as we showed for zinc) that may result in lower birth weight and length.
Carcinogenic effects of chemicals are usually assessed in two-year animal experiments with rodents. Alternative test methods replacing rodent bioassays or at least reducing the number of animals would be desirable. The pH 6.7 Syrian hamster embryo (SHE) cell transformation assay is a promising in vitro test system for the prediction of chemically-induced carcinogenicity. Good concordance between morphologic cell transformation and results from long-term rodent carcinogenicity studies is reported especially for aromatic amines. The aim of our present study was to establish and validate the SHE assay for further testing substances of this chemical class.

We conducted the assay with 2-naphthylamine, o-toluidine HCl, 2,4-diaminotoluene, p-phenylenediamine 2 HCl and aniline. In each assay 6 – 8 different concentrations of the test substance as well as negative (0.2% DMSO or medium) and positive controls (2.5 or 5 µg/ml benzo[a]pyrene) were used. After continuous incubation for 7 days in Petri dishes SHE cell colonies were fixed with methanol, dyed with Giemsa stain, and examined for morphologic transformation using a stereomicroscope.

For the carcinogenic arylamines 2-naphthylamine, o-toluidine HCl and 2,4-diaminotoluene concentration-dependent increases of morphologic transformation frequencies (MTF) were observed. MTF values of treated cultures differed significantly from those of the respective negative controls. The non-carcinogenic or suspected carcinogens p-phenylenediamine 2 HCl and aniline yielded negative results. For these two substances the MTF values were largely in the same order of magnitude as the corresponding negative controls.

We could show for the first time that aniline yields negative results after incubation for 7 days in the low pH SHE cell transformation assay which is thought to be more sensitive than pH 7.0 – 7.3 SHE assay. Currently aniline and p-phenylenediamine 2 HCl are rechecked with a short-term incubation (24 h) to verify the negative outcome of the experiments. So far our results indicate together with other published data that the SHE assay seems to be suitable for predicting the carcinogenic potential of aromatic amines.
PSYCHOSOCIAL RISKS AT THE WORKPLACE – AN INCREASING CHALLENGE FOR HEALTH PROTECTION

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In recent years scientific evidence has shown that psychosocial risks at the workplace can have adverse effects both on the health and well-being of the working people. Still the subject seems to be hard to handle. On the one hand the annual reports of the health insurance companies point to an increasing number of mental health disorders such as anxiety and depression. On the other hand evidence has shown that stress can also contribute to the development of physical disorders such as cardiovascular diseases or chronic back ache. In consequence employers are obliged “to ensure the safety and health of workers in every aspect related to the work” (as written in the Framework Directive on safety and health. Council Directive 89/391). National and international efforts are being done made to reduce psychosocial risks and to improve health and well-being at work. The German Social Accident Insurance Institution for the Raw Materials and Chemical Industry (Berufsgenossenschaft für Rohstoffe und Chemische Industrie, BG RCI) has developed several prevention tools to help employers and their employees to deal with psychosocial risks in the workplace such as seminars, projects or individual counselling.
Our body experiences hypoxia in different settings and through adaptation mechanisms reacts to the Hypoxic states. Hypoxia response system is a tissue-specific Oxygen-sensing system, which regulates the synthesis of a transcription factor known as hypoxia inducible factor 1 (HIF 1). This transcription factor controls the expression of many important genes that have impacts on both development and hypoxia related diseases. HIF 1 over expression may activate the transcription of genes (NOS2 and VEGF involved in angiogenesis; IGF-2 which contributes to the cell survival / proliferation, glucose transporters and glycolytic enzymes which promote metabolic adaptation to hypoxia).

Studies shows that HIF-1 over expression has been associated with increased patient mortality and treatment failure in clinical trials.

In several studies however, no change in performance of workers who are in good health as well as highly trained athletes who experience short-term normobaric hypoxia states have been suggested.

It can be argued that inter-individual variability in the adaptive response to hypoxia could represent non-physiological epigenetic factors or insensitivity of physiological markers to hypoxia-induced adaptation.

This presentation addresses the hypoxic situation in different environmental and occupational settings and discusses in detail the cellular, molecular, pathophysiological responses and adaptations of the body organs.

KEY WORDS: Normobaric hypoxia, HIF, cellular adaptation.
Nanotechnology was identified by Bayer Material Science (BMS) as a tool and a platform for various innovation and growth areas along the value chain. It can provide better product solutions in many sectors, including polymer and adhesive additives, nanocomposite thermoplastics and nano-modified coating systems. As part of its entry into this market, BMS has committed to an extensive Product Stewardship program to ensure safe handling and care for the environment. The development of nanomaterials is taking place within the chemicals industry’s Responsible Care® Global Charter framework.

A strong Product Stewardship program for nanomaterials and especially for Multi-Walled Carbon Nanotubes under the tradename Baytubes® was implemented. The aim is to ensure safe use of our products. This is achieved by installing strict safety standards and by addressing the knowledge gaps regarding health, safety and environmental (HSE) aspects of nanomaterials. These investigations focused on the characterization, the potential for exposition as well as the examination of the intrinsic toxicological and ecotoxicological profiles. In addition to internal work, BMS contributes to nanomaterial safety research projects funded by the German Ministry of Education and Research (BMBF), such as CarboSAFE, CarboTox and NanoGEM, which focus on the development of a broad scientific consensus on measurement methods and testing procedures for nanomaterial safety assessments.

The level of responsible care taken by all partners along the value chain will strongly influence the success of nanotechnology. In order to ensure the development of beneficial novel products and applications the industrial stakeholders have to ensure that the production, handling, transport and use of products of nanotechnology are safe.
EFFECTS OF VAPOURS AND AEROSOLS OF BITUMEN ON BIOMARKERS OF INFLAMMATION – ASSESSMENT OF IRRITATIVE EFFECTS ON THE AIRWAYS OF MASTIC ASPHALT WORKERS USING NON-INVASIVE METHODS


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Possible health hazards of vapours and aerosols of bitumen have been a subject of discussion for several years. Although an analysis of non-malignant diseases revealed an increased mortality from respiratory diseases in pavers and mastic asphalt workers, data on irritative effects of vapours and aerosols of bitumen in humans are limited. To assess irritative effects of exposure to vapours and aerosols of bitumen, a cross-sectional cross-shift study (the German Bitumen Study) was conducted with 320 workers exposed to vapours and aerosols of bitumen. The reference group consisted of 118 workers from outdoor construction sites without exposure to bitumen during the past five years. Air monitoring of vapours and aerosols of bitumen and polycyclic aromatic hydrocarbons (PAH) during the shift and biological monitoring of PAH metabolites pre and post shift revealed individual exposure levels. Personal monitoring of the 320 bitumen-exposed workers resulted in a median shift concentration of vapours and aerosols of bitumen of 3.46 mg/m³ (interquartile range (IQR) 1.8 to 5.9 mg/m³). Here we report on irritative effects based on the application of non-invasive methods pre- and post shift. We analysed the cellular and humoral composition of nasal lavage fluid (NALF) and induced sputum (IS) samples in order to assess inflammatory processes in the upper and lower airways. No significant differences between bitumen-exposed workers and the reference group, and no significant shift effect were observed on the upper airways using NALF analysis. In IS, the total cell count showed higher values in smokers than in non-smokers and in bitumen-exposed workers compared to the reference group. In addition, the concentrations of interleukin (IL)-8, total protein and matrix metalloproteinase-9 in IS were significantly higher in bitumen-exposed workers than in the reference group. However, the concentration of these three biomarkers in the IS samples were already higher in exposed workers before shift and did not show an increase during the shift. Therefore, the key finding of this aspect of the Human Bitumen Study is the detection of potentially (sub-)chronic irritative-inflammatory effects in the lower airways of bitumen-exposed workers.
DOSE-RESPONSE AT VERY LOW EXPOSURES: BIOLOGICAL RHYMES AND REASONS

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Risk assessment has been developed to address possible health risks at the very low exposures that are most relevant to people, whereas most of the dose-response data available are from high-exposure settings, such as the workplace and/or animal studies.

This presentation will address three different models and their assumptions currently used in risk assessments, including 1) linear (or pseudolinear), non-threshold model, 2) threshold models, and 3) other nonlinear models such as a biphasic or hormetic model, and their toxicological foundations. While the US Environmental Protection Agency default assumption is that no threshold exists for substances showing carcinogenic activity in animal experiments or epidemiology studies, the Agency has concluded that the linearized multi-stage model is inappropriate for a few carcinogens (e.g., dioxin, nitrilotriacetic acid, d-limonene). The European Union and many of its members make a distinction between carcinogens that are genotoxic and those believed to produce tumors by non-genotoxic mechanisms, and treat them differently with respect to risk assessment models.

Conversely, while many regulatory agencies generally assume thresholds for non-cancer endpoints, there is currently a debate that while a threshold may exist for certain chemicals at an individual level, the threshold differs among people and thus at the population level there is no threshold and even the smallest doses have some finite population risk (NRC 2009). Although using the various default approaches is often useful in the risk assessment process, it is important to understand the biological mode of action in assessing risk, particularly when extrapolating to the very low region of the dose-response curve. A more appropriate framework would start with an understanding of the biological pathways associated with the pathogenesis of any adverse effects and then integrate considerations of exposure, target-site dose, and timing with respect to life-stage sensitivity. Recent advancements in characterizing very low exposure concentrations, statistical models and in understanding modes of action have the potential for more robust epidemiological evaluation of populations exposed occupational- ly, environmentally or through consumer products to chemicals in very low concentrations.
CHEMICAL OCULAR BURNS: EXPERIMENTAL DATA AND CLINICAL IMPLICATIONS

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OBJECTIVE: The intra-ocular penetration of corrosive substances is poorly known. The kinetics of the diffusion through the cornea is difficult to measure and the effectiveness of the solutions of decontamination usually used has never been quantified up to now. The objective of this work is to specify the corneal penetration mechanisms of different chemicals as well as the mode of action of different decontamination solutions.

MATERIALS AND METHODS: Experiments were performed on rabbit corneas. After having exposed corneas to a chemical, corneas were rinsed using different tested solutions, recommended in the literature. Optical Coherence Tomography (OCT) made it possible to show chemicals penetration through corneas by following the ionic concentration increase in each corneal layers. The effectiveness of the rinsing solutions was determined by the number of remaining corneal cells within the cells cultures successively exposed to chemicals and rinsed.

RESULTS: OCT enabled us to visualize in real time the intraocular penetration of sodium hydroxide, hydrofluoric acid and sulphuric acid. We thus could specify the best time for an efficient decontamination. Cells cultures observations showed that corneal cells were able to survive in a medium at pH 9 or 10 during 1 hour. Nevertheless, 50% of cells are destroyed when pH is close to 5.

CONCLUSION: The experimental studies on chemicals penetration through cornea and on the effectiveness of the different rinsing solutions help to define the best decontamination solution. These studies must also contribute to the development of a guideline when first responders or ophthalmologists are faced with a chemical ocular burn.
DEVELOPMENT AND PILOT OF A LEADING HEALTH METRIC SCORECARD FOR THE UK CHEMICAL INDUSTRY

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The UK Chemical Industries Association (CIA) revised its 10-year sustainable development goals during 2010. The ten new goals include a sustainable occupational health management goal for its member companies: 'to have effective health systems in place, which maximise employee health and wellbeing in the workplace'.

Traditionally, the UK CIA has measured health performance by lagging metrics such as occupational illness frequency rate, obtained from the Indicators of Performance, which its members submit annually as part of their commitment to Responsible Care.

The new approach will now also focus on leading metrics, in which member companies assess and report preventive health programme performance using a scorecard derived from a self-assessment multiple choice questionnaire. The scorecard addresses the degree of implementation of 14 aspects of preventive workplace health programmes grouped under five dimensions: 'Health Leadership', 'Health Organisation and Planning', 'Health and Business Performance', 'Health Hazard Exposure Control' and 'Health Exposure Monitoring'. Targets will be set for the proportion of member companies to achieve specified levels of performance on the scorecard 'A' (Advanced) to 'D' (Developing) rating scale for each dimension by 2020.

The leading health metric scorecard will be described during the presentation and the results of a pilot evaluation conducted in a multi-national chemical manufacturing company during 2010 will be discussed and presented.
Nanoparticles when inhaled can deposit deep in the lung. Depending on where they deposit, the nanoparticles can interact with the mucous lining fluid of the airways possibly causing inflammation. On the other hand nanoparticles hold promise as therapeutic agents and the lungs are an attractive route for non-invasive drug delivery.

In the context of medical research, especially for inhalation experiments and toxicological assessments, particle size and surface area of the nanoparticles are important characteristics and it is important to have a stable particle source for experiments.

We will present a nanoparticle generator that can generate a constant output of nanoparticles (20 nm - 200 nm) of various materials. Particles are generated via spark discharge, i.e. using high-voltage but low power between two electrodes leads to repeated, short-lived thermal plasmas evaporating small areas from the electrodes. The method can be applied to any conductive material including carbon and semiconductors. Spark discharge has also successfully been used for alloying materials, even if they are immiscible in the bulk phase. So by simply changing the electrode material a chemically different material can be evaporated to form nanoparticles and then used in the experiment.

Whereas mechanical milling requires the use of very high energy inputs as well as stabilizing agents in a dispersion, here the main input is electrical power for the discharges and the pumps and the particles are generated fresh without need of additives to prevent agglomeration. In comparison with other particle generation techniques this nanoparticle generation process is very versatile and reliable. It avoids chemical precursors and solvents while fully recycling the necessary inert carrier gas resulting in minimal impact on the environment.

We will show measurements with our U-SMPS system of particle size distributions obtained with this spark generator using different electrode materials.
OCCUPATIONAL EXPOSITIONS TO DANGEROUS PRODUCTS IN VIEW OF THE POISONS INFORMATION CENTRE FREIBURG

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(1) Poisons Information Centre, Centre for Pediatrics and Adolescent Medicine, University Medical Centre, Freiburg, Germany

INTRODUCTION: The Poisons Information Centre Freiburg (VIZ) serves a population of 10.5 million in southwest Germany. Most queries are about accidents in domestic surroundings. Since the VIZ provides a twenty-four hours a day service it can provide fast information in occupational expositions to dangerous substances also. We studied which occupational injuries caused a consultation of the poisons information centre.

METHODS: Retrospective analysis of the poisons centre’s data base from 2006 to 2010.

RESULTS: The Search retrieved 1846 occupational expositions. That is 2.0 % of all cases. Follow up information was available in 305 cases. 65 (21 %) of these 305 patients showed moderate or severe symptoms. In 72 % of the cases with minor symptoms but in 89 % of the cases with more than minor symptoms the chemical in question was considered the cause of the symptoms. Main cause of at least moderate severe courses was inhalation of toxic (irritant) gases. The only fatality was due to inhalation of toxic gases in a cesspool. Another prominent problem was contact to corrosive cleaners (10 cases with at least moderate symptoms). 4 persons suffered aspiration injury while performing fire breathing.

CONCLUSION: Occupational expositions to toxic or corrosive substances are a minor part of the work of the VIZ. Irritant or toxic gases and corrosives e. g. drain cleaners caused most of the moderate or severe occupational poisonings reported to the poisons centre.
THE CARCINOGENICITY OF SHIFT WORK – THE IARC EVALUATION AND BEYOND

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(1) International Agency for Research on Cancer (IARC), World Health Organization (WHO), Lyon, France

In October, 2007, the International Agency for Research on Cancer (IARC/WHO) convened a Monographs meeting to assess the carcinogenicity of shift-work. About 15–20% of the working population in Europe and the USA is engaged in shift-work that involves nightwork.

In 2007, six of eight epidemiological studies from various geographical regions, most notably two independent cohort studies of nurses engaged in shift-work at night have noted a modestly increased risk of breast cancer in long-term employees compared with those who are not engaged in shift-work at night. These studies are limited by potential confounding and inconsistent definitions of shift-work.

Several different rodent models have been used to test the effect of disruption of the circadian system, reduced nocturnal melatonin concentrations or removal of the pineal gland on tumour development and most showed increases in the incidence or growth of tumours.

Exposure to light at night disturbs the circadian system with alterations of sleep-activity patterns, suppression of melatonin production, and deregulation of circadian genes involved in cancer-related pathways. In animals, melatonin suppression can lead to changes in the gonadotrophin axis. In humans, sleep deprivation and the ensuing melatonin suppression lead to immunodeficiency.

On the basis of “limited evidence in humans for the carcinogenicity of shift-work that involves night-work”, and “sufficient evidence in experimental animals for the carcinogenicity of light during the daily dark period (biological night)”, the Working Group concluded that “shift-work that involves circadian disruption is probably carcinogenic to humans” (Group 2A).

Since 2007 several new studies, particularly on shift-work and breast cancer, have been published or presented at international meetings. Their results as well as recent activities on exposure assessment will also be presented.
OCCUPATIONAL EXPOSURE LIMITS AND REACH

**Stropp, G.** (1)

(1) Institute for Toxicology, Department of Product Stewardship Industrial Chemicals & Operations at Bayer Schering Pharma AG, Wuppertal, Germany

REACH Regulation requires the registrant to determine "derived no-effect-levels" (DNELs) when preparing the chemical safety report. DNELs shall be established reflecting the likely routes, duration and frequency of exposures. The risk characterisation consists of a comparison of human exposures with the appropriate DNELs. When DNELs are achieved the risks to humans are considered to be adequately controlled. By that the DNELs serve as benchmarks for the derivation of risk management measures.

For the occupational setting, inhalation is a major route of potential exposure, and therefore typically DNELs have to be derived also for the inhalation route. Occupational exposure limits (OELs) are available for a number of chemicals, therefore the relationship between the DNEL for long term inhalation exposure and national or international OELs is of scientific interest and of practical relevance. Guidance is given by the European Chemicals Agency (ECHA) concerning DNEL derivation when an occupational exposure limit is available and by the German Committee on Hazardous Substances (AGS) for using REACH-information for health and safety work, e.g. in case that both a national OEL as well as DNELs is available. Basic principles will be demonstrated in the presentation, and background information for derivation of Occupational Exposure Limits and "derived no-effect-levels" will be given.
BIOLOGICAL EFFECTS OF EUROPIUM (III) CHLORIDE HEXAHYDRATE (EUCL3•6H2O) IN RATS AFTER SINGLE ORAL DOSES

(1) Osaka Medical College, Department of Hygiene and Public Health, Takatsuki City, Osaka, Japan

Europium (Eu) is widely used as a key ingredient in the new type long-life low-energy mercury-free compact fluorescent lamps, red phosphors for television (TV), personal computer (PC) display panel and luminescent materials. Thus, Eu can pose a potential health hazard as environmental pollutant of concern associated with the increasing electric waste of broken lamps, TV and PC. Electrical workers are expected from occasional exposure associated with industrial manufacturing process, however report of Eu health impacts is limited.

The purpose of the present study is to explore the Eu elimination via bloodstream to urine and Eu induced renal effect along with the administrated Eu dose (A-Eu) by animal experiment. To achieve the purpose, several groups of rats were administered Europium (III) chloride hexahydrate (EuCl3•6H2O) and cumulative urine samples at 0-24h (CU0-24h) and blood samples at twenty-four hours after administration (B24h) were collected. Eu elimination was evaluated by Eu concentration (UC-Eu), excretion (UE-Eu) of CU0-24h, percentage of Eu excreted in CU0-24h (%UE-Eu) and blood Eu concentration of B24h (B-Eu). UC-Eu and B-Eu were determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES). Eu induced renal effect was evaluated by urine volume (UV), creatinine (Crt), β-2-microglobulin (β2-MG) and N-acetyl-β-D-glucosaminidase (NAG) of CU0-24h. UC-Eu was converted to UE-Eu and %UE-Eu by UV and A-Eu.

B-Eu showed low Eu distribution to B24h with average of 77.5 µg/L for groups. Although UC-Eu and UE-Eu showed dose-dependent increase, percentage of Eu excreted in CU0-24h (%UE-Eu) showed dose-dependent decrease with the average of 0.36% for groups. The administration of Eu induced a significant decrease of Crt and a significant increase of UV and NAG and β2-MG.

Rare earth elements (REEs) including Eu are believed to make the formation of colloidal conjugates that deposit in reticuloendothelial system and glomeruli. This specific reaction may contribute to low Eu bioavailability and renal function disturbance. Despite the low Eu bioavailability, the high performance of ICP-AES makes UC-Eu and B-Eu useful tools for Eu exposure monitoring. The results of this experiment will be of great importance for future studies on REEs related health impacts.
Wiener, A. (1)
(1) Institute of Occupational and Environmental Medicine, Rambam Medical Center, Haifa, Israel

Environmental toxicology, a branch of ecology, aims to characterize, understand, and predict deleterious effects of harmful chemicals on biological systems. It involves the study of sources, pathways, transformations, and impacts of industrial, agricultural pollutants and natural biotoxins on biota plants and animals at the population, community and ecosystem levels. Rachel Carson first drew our attention to the harmful impacts of pesticide exposures on untargeted victims. Later, catastrophic industrial and agricultural pollution of air, soil and water have caused mass morbidity and mortality among marine biota, birds and terrestrial wildlife and livestock. Persistent organic pollutants (POPs) were found to act as carcinogens, endocrine disruptors, neurotoxins and immunosuppressants to many species. The noxious effects of many anthropogenic toxicants have been gradually decreased by regulatory restrictions. Meanwhile, new environmental risks continue to emerge. The growth of nanotechnology may raise new hazards, albeit not well defined. Overuse of fertilizers is increasing nutrient runoff, resulting in harmful algal blooms (HAB) in estuaries and coastal regions worldwide. Such HABs can disrupt marine habitats with dire economic impacts to coastal businesses such as shellfish farming and fishing due to the noxious effects to seafood of these species. Public health concerns over HAB-related shellfish diseases have become a global issue. Algal biotoxins are capable of entering the aquatic food chain, ultimately becoming concentrated in shellfish and finfish, which if consumed by humans, can cause significant illness. In addition, HABs may also affect ecosystems by causing impaired growth and fecundity in grazing populations or, anoxic or hypoxic conditions following the decline of large HABs. Recently HABs have been occurring in freshwater lakes, causing severe human illnesses by various toxins. Some of these were found to be stable in water even after total disappearance of the algae. Such toxins were detected also in drinking water. Another agro-chemical risk relates to application of Selenium-rich phosphate-based fertilizers, which can cause lethal disease among livestock. Finally, environmental exposure to anthropogenic Endocrine Disruptors (ED) is of growing concern, especially regarding the risk of consuming xenoestrogens. These EDs threaten fecundity in some species rendering them as candidates for extinction. Exposure to some EDs might alter fat accumulation in certain species. It has been speculated that human exposure to EDs might be related to the obesity epidemic in Western societies. Past environmental concerns over agricultural pollution was manageable by regulatory legislation. Presently, many deleterious effects are increasingly difficult to regulate. Responsiveness to public concerns involves cost/benefit analysis, including the difficult choices between food production and environmental protection. Pesticides use continues even after their hazards are presented to regulatory bodies; pesticides may not be required to be tested for certain hazards, e.g., ED, for which adequate testing standards have yet to be fully developed. As yet, an effective method to prevent HABs resulting from fertilizer runoff has not been established. Best management practices are being investigated and have been shown to reduce phosphate runoff into the Lake Erie watershed of Ohio in the U.S..
ABERRANT METHYLATION AND EXPRESSION OF TUMOR SUPPRESSOR GENE P15 AND P16 IN BENZENE POISONING

Xing, C. (1) (2), Wang, Q. (3), Li, G. (1)
(1) National Institute of Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention, Beijing, China
(2) School of Public Health, Peking University, Beijing, China
(3) Beijing Institute of Genomics, Chinese Academy of Sciences, Beijing, China

Benzene is an important industrial chemical and a universal environmental pollutant that causes hematotoxicity and acute myeloid leukemia (AML). The underlying mechanism of benzene poisoning (BP; i.e. hematotoxicity), however, is poorly understood. In AML, DNA hypermethylation has shown to be the primary mechanism that leads to the loss of expression of p15 and p16. Previously, we found a borderline significant down-regulation of p15 and p16 in BP patients, and a negative correlation between p16 expression and methylation of specific promoter CpG in a small case-control study in which the control is benzene exposed workers. These data suggest that epigenetic changes may be a potential mechanism underlying hematotoxicity of benzene. To further explore whether benzene negatively affects the expression of p15 and p16 through DNA methylation in promoter regions, a relative large cohort were recruited in this study including 20 cases of BP, 17 healthy benzene-exposed workers who were matched for age (± 5ys), sex, working duration and job title with BP and 19 matched unexposed controls from Tianjin, China. qRT-PCR and Bisulfite-PCR pyrosequencing were used for detecting expression and methylation changes. Comparing to the unexposed control, both p15 and p16 mRNA expression levels were significantly down-regulated in BP patients (p<0.00001, p<0.00001, respectively) and also in benzene-exposed workers (p<0.01, p<0.01, respectively). The methylation level at the second CpG site within p16 promoter region was significantly higher in BP compared with unexposed control (1.5% and 0.0%, p<0.05). For the third CpG site of p16, it was significantly higher in BP than in benzene-exposed group (4.8%, 2.3%, p<0.01) and also higher than in unexposed control (4.8%, 2.1%, p<0.01). A significantly negative correlation was found between mRNA expression and methylation at the second CpG site (Pearson r= -0.34, p=0.013), but no statistically significant at the third CpG site of p16 (Pearson r= -0.23, p=0.096). The methylation level of p16 at second and third CpG site was positively correlated (Pearson r=0.34, p=0.014). The second CpG site is located within the consensus binding sequence for the deformed epidermal autoregulatory factor 1 (DEAF-1). The Third CpG site is located within the consensus binding sequence for olfactory neuron-specific transcription factor. In order to examine whether benzene directly affects gene expression of p15 and p16, we cultured human lymphocytes as whole blood in the presence of hydroquinone (HQ), the major metabolite leading to hematotoxicity of benzene. The expression of p15, but not p16, was significantly downregulated 24 hours after HQ exposure. Our report suggests that chromatic benzene exposure induces down-regulation of p15 and p16 at mRNA level among BP patients and benzene-exposed workers. Benzene metabolite HQ may directly induce downregulation of p15. Hypermethylation in promoter CpG islands is likely to contribute to the decreased expression of p16. Further in-depth studies are needed to fully understand the molecular mechanism involved in the tumor-suppressor gene inactivation in benzene-related diseases.
MANAGEMENT OF CHEMICALS: THE GLOBAL CONTEXT

Younes, M. (1)
(1) World Health Organization (WHO), Geneva

While chemicals play an integral role in society due to the increasing dependence on them in many products, services and processes, and while they are integral to the development of most sectors, they may, if improperly or inadequately managed, pose serious threats to environmental integrity and human health. This requires the establishment of strong, enforceable management structures at various levels. In recent years, there has been a marked increase in the production of chemicals worldwide, with developing countries accounting for an increasing percentage, with an emphasis on bulk chemicals. This, together with other factors including the transboundary movements of chemicals, the need to share the burden of chemicals assessment, and the potential trade implications, are among the reasons why action on chemicals management is required at the global level.

The keynote address will discuss key actions at international level following the 1972 United Nations Conference on the Human Environment in Stockholm, agencies involved in international work on chemicals management, relevant multilateral environmental agreements, and key features of the Strategic approach to International Chemicals Management (SAICM). Challenges and global strategies will be presented.
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WINNER OF AWARDS AT MEDICHEM 2011

Winner of the MEDICHEM Scholarship Award 2011

Dr. Martina Piasek Institute for Medical Research and Occupational Health, Zagreb, Croatia

Dr. Caihong Xing National Institute of Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention, Beijing, China

Granted the MEDICHEM Young Professionals Award 2011

Dr. Keiichi Fujimoto Osaka Medical College, Department of Hygiene and Public Health, Osaka, Japan

Prof. Dr. Ehsan Habibi Isfahan University of Medical Sciences, Isfahan, Iran

Dr. Amir Radfar Babol University of Medical Sciences, Babol, Iran
LIST OF KEYNOTE AND INVITED SPEAKERS

We are pleased to confirm that the following A-List of brilliant speakers will present at MEDICHEM 2011
(at www.medichem2011.org you can find under the respective links in the speakers list at the right side of the page more information on each speaker or chair).

Dr. Thomas H. Brock
Head, Department of Hazardous Substances and Biological Agents at Work, BG RCI (German Social Accident Insurance for the Raw Materials and Chemical Industry), Heidelberg, Germany

Dr. Vincent Castranova
NIOSH (National Institute for Occupational Safety and Health), Chief of the Pathology and Physiology Research Branch, Morgantown, USA

Dr. William Murray Coombs
Dow, Regional Health Director - Middle East, Africa & India, Sentrachem Limited, Bryanston; South African Society of Occupational Medicine, South Africa

Prof. Dr. Ken Donaldson
Director of the Edinburgh Lung and Environment Group Initiative (ELEGI) Laboratory, Queen’s Medical Research Institute, MRT Centre for Inflammation Research, University of Edinburgh, Edinburgh, Scotland, UK

Dr. Andreas Flückiger
Head of Roche’s Corporate Health Protection Department, Hoffmann-La Roche Ltd., Basel, Switzerland

Prof. Dr. Heidi Foth
Director of the Institute of Environmental Toxicology Martin-Luther University Halle-Wittenberg, Halle / Saale, Germany

Prof. Dr. Helmut Greim
Member of SCOEL (Scientific Committee on Occupational Exposure Limits), Member of the Risk Assessment Committee of ECHA (European Chemicals Agency in Helsinki, Finland), Institute of Toxicology and Environmental Hygiene, Technical University, Munich, Germany

Prof. Dr. Andrea Hartwig
President of the "MAK-Commission" (Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area), Professor at the Karlsruher Institute of Technology (KIT), Institute of Applied Biosciences, Department of Food Sciences and Toxicology, Karlsruhe

Prof. Dr. Dr. Uwe Heinrich
Head of Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Hannover, Germany

Dr. Heiko U. Käfferlein
Head, Centre of Toxicology, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of Ruhr University Bochum (IPA), Bochum, Germany

Dr. Michael Nasterlack
Vice President, Occupational Medicine & Health Protection, BASF SE, Ludwigshafen, Germany

Prof. Dr. Günter Oberdörster
Professor of Toxicology, Department of Environmental Medicine, University of Rochester, Director of the University of Rochester-EPA Ultrafine Particle Center, Head of the Pulmonary Core of the NIEHS Center Grant Rochester, Rochester, USA

Dipl.-Psych. Roland Portuné
BG RCI (German Social Accident Insurance Institution for the Raw Materials and Chemical Industry), Department of Occupational Psychology, Heidelberg, Germany

Prof. Dr. Kurt Straif
Head of the Section of the IARC Monographs, International Agency for Research on Cancer (IARC), World Health Organization (WHO), Lyon, France

Dr. Gisela Stropp
Head, Institute for Toxicology, Department of Product Stewardship Industrial Chemicals & Operations at Bayer Schering Pharma AG, Chairperson of the subcommittee on “Hazard Risk Assessment” of the German Advisory Committee on Hazardous Substances (AGS-UAIII) Bayer Schering Pharma AG, Wuppertal, Germany

Dr. Avi Wiener
Medical Director, Institute of Occupational & Environmental Medicine, Rambam Medical Center, Haifa, Israel

Prof. Dr. Maged Younes
Director Food Safety, World Health Organization (WHO), Geneva, Switzerland. Former Head UNEP (United Nations Environment Programme), Chemicals Branch, Geneva, Switzerland
LIST OF CHAIRPERSONS AT MEDICHEM 2011

We are pleased to confirm that the following A-List of brilliant chairpersons will support the success of the congress.

(at www.medichem2011.org you can find under the respective links in the speakers list at the right side of the page more information on each speaker or chair).

Shift work and cancer – Current discussion
Chair:
Dr. Michael Nasterlack
Vice President,
Occupational Medicine & Health Protection, BASF SE, Ludwigshafen, Germany

and

Dr. Abed bin Onn
Subang Jaya Selangor, Malaysia

Case Reports – Interesting observations in the occupational health world
Chair:
Dr. Andreas Flückiger
Head of Roche’s Corporate Health Protection Department
Hoffmann-La Roche Ltd., Basel, Switzerland

and

Dr. Diane J. Mundt
ENVIRON International Corporation, Boston, USA

Toxicology – New results, emerging risks
Chair:
Prof. Dr. Günter Oberdörster
Professor of Toxicology
Department of Environmental Medicine, University of Rochester
Director of the University of Rochester-EPA Ultrafine Particle Center
Head of the Pulmonary Core of the NIEHS Center Grant Rochester, Rochester, USA

and

Dr. Kenneth A. Mundt
Principal and Director of Epidemiology
ENVIRON International Corporation, Boston, USA
Regulation in occupational health – Recent developments and REACH – Impact on occupational and environmental health

Chair: Prof. Dr. Andrea Hartwig
(Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area)
Professor at the Karlsruhe Institute of Technology (KIT)
Institute of Applied Biosciences, Department of Food Sciences and Toxicology, Karlsruhe, Germany
and
Prof. Dr. Heidi Foth
Director of the Institute of Environmental Toxicology
Martin-Luther University Halle-Wittenberg, Halle / Saale, Germany

Strategic Approach to International Chemicals Management (SAICM) – Status and developments

Chair: Prof. Dr. Maged Younes
Director Governing Bodies (GBS), Director Food Safety World Health Organization (WHO), Geneva, Switzerland and former Head UNEP (United Nations Environment Programme), Chemicals Branch, Nairobi, Kenya
and
Prof. Dr. Helmut Greim
Member of SCOEL (Scientific Committee on Occupational Exposure Limits)
Member of the Risk Assessment Committee of ECHA
(European Chemicals Agency in Helsinki, Finland), Munich, Germany

8.30 – 10.00 / 10.30 – 12.30

Nanotechnology – Challenges and solutions

Chair: Prof. Dr. Dr. Uwe Heinrich
Head of Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Hannover, Germany
and
Dr. Maren Beth-Hübner
BG RCI (German Social Accident Insurance Institution for the Raw Materials and Chemical Industry), Department of Hazardous Substances and Biological Agents at Work, Heidelberg, Germany
Adverse effects on employees, customers and the general public – Preventive measures
Chair:
Dr. Michael Nasterlack
Vice President, Occupational Medicine & Health Protection, BASF SE, Ludwigshafen, Germany
and
Dr. William Murray Coombs
Dow, Regional Health Director - Middle East, Africa & India, Sentrachem Limited, Bryanston, South Africa

Biomarkers – Progress in research and practical application
Chair:
Dr. Heiko U. Käfferlein
Head of Centre of Toxicology, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance Institute of Ruhr University Bochum (IPA), Bochum, Germany
and
Dr. Martina Piasek
Institute for Medical Research and Occupational Health, Zagreb, Croatia

Occupational health – Trends and evolution
Chair:
Dr. Steffen Hitzeroth
Medical Director Occupational Health Procter & Gamble Service GmbH, Schwalbach a. Ts., Wiesbaden, Germany
and
Dr. Andreas Flückiger
Head of Roche’s Corporate Health Protection Department Hoffmann-La Roche Ltd., Basel, Switzerland
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- Professor Dr. Alfred Thiess, Founder and Honorary President of MEDICHEM
- Dr. Harald Wellhäußer, BG RCI

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- Professor Dr. Alfred Thiess, Founder and Honorary President of MEDICHEM
- Dr. Harald Wellhäußer, BG RCI

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- Annett Bruhns, BG RCI, Langenhagen
- Helga Dykema, BG RCI, Heidelberg
- Gabriele Haass, BG RCI, Heidelberg
- Marion Schuhmacher, BG RCI, Heidelberg

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- Marcin Czerwinski, BG RCI, Langenhagen
- Holger Imhoff, BG RCI, Langenhagen
- Doris Keller*, BG RCI, Heidelberg
- Christoph Mann, BG RCI, Heidelberg
- Ilka Merkschien, BG RCI, Langenhagen
- Bernd Nellinger, BG RCI, Mainz
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SOCIAL PROGRAM AND TOURS AT MEDICHEM 2011

The congress social events (all included in the conference fee) will feature the Opening Ceremony, framed by music, with cold and warm buffet reception on Thursday,

an organ concert in the Church of the Holy Spirit in the heart of Heidelberg's famous Old Town and the reception by the Mayor of Heidelberg at the Town Hall just opposite the church on Friday,

as well as the Champagne reception on the Castle Gallery, the Gala Dinner in the Castles Ottheinrichsbaun, and the Giant Firework display on Saturday. Also included in the conference fee is an Excursion to BASF SE, Ludwigshafen, which is the cradle of MEDICHEM in the year 1972, on invitation of BASF on Thursday morning, before the official opening of the Congress on Thursday evening.

With this all-inclusive conference package we hope that all participants not only benefit from a productive and profitable congress but also enjoy a few memorable days in Heidelberg in the early summer of 2011. We greatly look forward to welcoming you at MEDICHEM 2011 in Heidelberg, Germany.

Excursions for Accompanying Persons (to be booked via Registration Form)

**River Neckar Valley Roundtrip, Friday, 03.06.2011**

**Time:** 9:30 - 13:00 hrs. (Minimum of participants: 15 persons)

Beginning/end of tour: Heidelberg Marriott Hotel

Pick up by boat directly at the hotel and trip to the public landing stage at the convention center. Start for the 1,5 hours regular boat trip along the most beautiful part of the Neckar valley to the 4-castles-town Neckarsteinach. Pick up by our bus in Neckarsteinach and trip to fortress Dilsberg - short visit of this picturesque, medieval village with it's lovely view down the river Neckar valley. Return trip to Heidelberg. Services: English speaking tourist guide, boat trip, coach hire.

**Price:** Euro 45,00 per person
Historical city of Heidelberg, Friday, 03.06.2011

Time: 14:30 - 17:00 hrs. (Minimum of participants: 15 persons)

Beginning/end of tour: Heidelberg Marriott Hotel

Guided walking tour through the historical part of the city incl. visit of the Old University (University Museum, Students’ Prison, eventually, if free, historical Assembly Hall “Alte Aula”), University Library, Old Bridge. Services: English speaking tourist guide, transportation downtown and back to hotel, entrance fee Old University.

Price: Euro 25,00 per person

Excursion Speyer - Schwetzingen, Saturday, 04.06.2011

Time: 9:00 - 13:00 hrs. (Minimum participants: 15 persons)

Beginning/end of tour: Heidelberg Marriott Hotel

Bustrip to Speyer, which is a real place of German history. Towering above this old imperial city is the splendid romanesque cathedral, 1000 years old and quite unique. In the historical old city and in the part of the old Jewish quarter you also find a Jewish ritual bath (Mikwe), one of the oldest, still conserved in its original form. Continue trip to Schwetzingen, former summer residence of the Prince Electors of the Palatinate. Visit of the castle gardens which are one of the most beautiful in Germany. Services: English speaking tourist guide, coach hire, entrance fees Speyer (cathedral crypt/Jewish bath), entrance fee castle gardens Schwetzingen.

Price: Euro 53,00 per person

Note: Realization of a tour is only guaranteed if the indicated minimum number of participants is reached. If this is not the case the paid money will be refunded. If you would like to book a pre- or post-congress tour you could do so on your own responsibility: http://www.touring-travel.eu/?id=6 or http://www.touring-travel.eu/index.php?id=18.
Church of the Holy Spirit (Heiliggeistkirche)

Organ Concert with Wenzel Hübner

18.00 h (Entrance from 17.45 to 18.15, then door will be closed)

Johann Sebastian Bach
(21.3.1685, Eisenach - 28.7.1750, Leipzig)

Toccata and Fugue D-Minor
BWV 565

Jesus bleibet meine Freude
from Cantata 147

Charles Francois Gounod
(17.6.1818, Paris - 17.10.1893, Paris)

Ave Maria
(Meditation on the most noted prelude of J. S. Bach)

Joseph Gabriel Rheinberger
(17.3.1839, Vaduz - 25.11.1901, München)

Introduction, Intermezzo and Pasacaglia E-Minor
Opus 132

Padre Davide da Bergamo
(21.1.1791, Zanica - 24.7.1863, Bergamo)

Elevazione B-flat-Major

Nicolas Jacques Lemmens
(3.1.1823, Zoorle-Parwijs (Antwerpen) - 30.1.1881, Mecheln)

Prière F-Major

Frederick Scotson Clark
(16.11.1840, London - 5.7.1883, London)

Marche A-Major

Maria Auguste Durand
(18.7.1830, Paris – 31.5.1909, Paris)

Allegretto a-Minor

Charles-Camille Saint-Saëns
(9.10.1835, Paris - 16.12.1921, Algier)

Le Cygne - The Swan
from Le Carneval des animaux

Félix Alexandre Guilmant
(12.3.1837, Boulogne-sur-mer - 30.3.1911, Paris)

Grand Triomphal Chorus A-Major
Opus 47,2

Wenzel Hübner was born in Heidelberg 1950. At the age of 15 he started as a church organist. Besides this he studied Mathematics, Physics and Chemistry. As a mathematician he worked at the German Cancer Research Center (DKFZ) in Heidelberg and at SAP in Walldorf. In 1991 he changed to the world famous Stumm-Organ (1782) with 5116 pipes in the former Abbey Church of Amorbach in the Odenwald. There he played nearly 8000 concerts for people from all over the world. Some well known notabilities listened to his concerts (i.e. H.R.H. Juan Carlos, King of Spain, H.R.H. Prince Philipp from G.B., H.R.H Crown Prince Shwebomin of Burma, H.H. Prince Aga Khan, Helmut Kohl). He is author of the largest organ inventory “21000 Orgeln in aller Welt” (21000 Organs World Wide).
ABOUT HEIDELBERG AND HOW TO GET THERE

World-famous castle and landmark sites

- Germany’s oldest university: 625th anniversary in 2011
- 145,000 inhabitants
- Pioneering research and science institutes
- 9 Nobel laureates
- Symbol of the German Romantic Movement and inspiration to numerous writers and poets
- A city in balance with nature
- Mediterranean climate and vegetation
- Lively hub of the Rhine-Neckar metropolitan region

The city of Heidelberg, home to Germany’s oldest university founded in 1386, celebrating its 625th anniversary in 2011, with its romantic townscape is an event in itself. The harmonious ensemble of the world’s most famous castle ruins, the Old Town and the Neckar river nestled amongst the hills already inspired the painters and poets of 19th century Romanticism. Heidelberg’s fascination continues until today for millions of visitors from all over the world.

Heidelberg is located approximately 80 km to the south of Frankfurt. Getting to and from Heidelberg is simple by either plane, train or road. From Frankfurt airport to Heidelberg we recommend to book the TLS Transfer door-to-door shuttle-service (https://www.tls-heidelberg.de/index.php/) (Euro 33.00 one way), which brings you directly to the hotel you booked and back from there to the airport. With the following links you can book your flights (http://www.flugsupermarkt.com/), and book your train (http://reiseauskunft.bahn.de/bin/query.exe?st=1), and find your car route (http://www.viamichelin.de/).

For English information about getting to Heidelberg and away (http://www.e-heidelberg.com/facts/#top), as well as about visitor attractions, restaurants, bars and useful facts for the visitor please click http://www.e-heidelberg.com/.

Useful English information about sightseeing in Heidelberg with beautiful pictures and short descriptions you will find here http://www.visit-heidelberg.com/tours/tours.htm.

Helpful English information about the history of Heidelberg, the student restaurants, the region, and the attractions of Heidelberg with many photos please find under http://www.historicgermany.com/3551.html, and nice picures about all main attractions in Heidelberg with very short English information http://www.galenfrysinger.com/heidelberg.htm.

A suggestion for 3 days in Heidelberg with walking tours for two days and excursions out of town for the third day is given here http://archives.starbulletin.com/2003/02/02/travel/story1.html.
NUMBERS AND DETAILS OF MEDICHEM 2011
(as at May 28 2011)

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NUMBERS AND DETAILS OF MEDICHEM 2011
(as at May 28 2011)

Participants

Participants (total) 218
- Congress Participants 165
- Accompanying Persons 53

New Members of MEDICHEM via MEDICHEM 2011 23

Contributions

Abstracts 55
- Posters 11
- Lectures 44

Oral Contributions (total) 56
- Keynotes 7
- Invited Lectures 11
- Free Communications 27
- Welcome Notes 7
- Introductions 3
- Moderation 1

Speakers (total) 51

Authors 119

Chairpersons 17
NUMBERS OF MEDICHEM 2011 - Countries

Countries represented at MEDICHEM 2011 (total) 30

Participants of each Country represented at MEDICHEM 2011 (without accompanying persons)

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</tbody>
</table>

Total 165
NEW MEMBERS OF MEDICHEM VIA MEDICHEM 2011

The Organizers wish to welcome the 23 new Members in the "MEDICHEM Family"

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USA
stout.r@pg.com

Prof Dr Kurt Ulm
Klinikum rechts der Isar
Ismaningerstr. 22
81675 München
Germany
kurt.ulm@tum.de
<table>
<thead>
<tr>
<th>EXTRACT OF</th>
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Registration Form

Title/Form of Address
- [ ] Prof
- [ ] Dr
- [ ] Mr
- [ ] Mrs
- [ ] Ms

Gender
- [ ] Male
- [ ] Female

Family Name/Last Name/Surname

Prefix (e.g. van, von, de)

First Name

Organization/Institute/Company Name

Organization/Institute/Company Address

Organization/Institute/Company City

Postcode

Country

E-mail-address
(Please confirm your e-mail-address.)

Contact Phone Number
 Internacional Code | City Code | Dialing Code

Mobile Phone Number
 Internacional Code | City Code | Mobile Phone Number

Conference Fees
- [ ] MEDICHEM Member
- [ ] Applicant for MEDICHEM Membership
- [ ] Non-Member
- [ ] Retired MEDICHEM Member
- [ ] Accompanying Person

Early registration
- [ ] (15 June 2010 – 15 March 2011)
- [ ] € 590.00
- [ ] € 650.00
- [ ] € 250.00
- [ ] € 100.00

Late registration
- [ ] (16 March 2011 – 15 May 2011)
- [ ] € 690.00
- [ ] € 750.00
- [ ] € 350.00
- [ ] € 120.00

I register as/for
- [ ] MEDICHEM Member*
- [ ] Retired MEDICHEM Member*
- [ ] Non-Member of MEDICHEM*
- [ ] Accompanying Person**

Application for MEDICHEM Membership
I wish to become a member of MEDICHEM and undertake to pay the annual subscription of € 40.00.
(Please fill in the membership application form on the website under "Conference Fees and Registration" and send to medichem2011@bgrci.de.)

Data of Accompanying Person:

Title/Form of Address
- [ ] Prof
- [ ] Dr
- [ ] Mr
- [ ] Mrs
- [ ] Ms

Gender
- [ ] Male
- [ ] Female

Family Name/Last name/Surname

Prefix (e.g. van, von)

First Name

Date of Registration
(yyyy-mm-dd)

Total Amount to be Paid
(You will receive a bill which has to be paid within 14 days to make registration valid.)

Dietary Requirements Delegate
- [ ] No restriction
- [ ] Vegetarian

Dietary Requirements Accompanying Person
- [ ] No restriction
- [ ] Vegetarian
<table>
<thead>
<tr>
<th>Registration Form</th>
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</thead>
<tbody>
<tr>
<td><strong>I have submitted an abstract</strong></td>
</tr>
<tr>
<td>[ ] Yes</td>
</tr>
<tr>
<td><strong>I apply with my abstract for</strong> (If awarded, registration costs will be refunded in the amount of the award)</td>
</tr>
<tr>
<td>[ ] MEDICHEM Prize</td>
</tr>
<tr>
<td><strong>I will attend the Excursion to BASF SE on 2 June 2011, 9 a.m. to 3 p.m., on invitation of BASF SE</strong></td>
</tr>
<tr>
<td>[ ] Yes</td>
</tr>
<tr>
<td>[ ] Accompanying person</td>
</tr>
<tr>
<td><strong>I will attend the opening ceremony, framed by music, with welcome addresses and reception with cold and warm buffet, on 2 June 2011, 7 to 10 p.m.</strong></td>
</tr>
<tr>
<td>[ ] Yes</td>
</tr>
<tr>
<td>[ ] Accompanying person</td>
</tr>
<tr>
<td><strong>I will attend the organ concert in the Church of the Holy Spirit (6 to 7 p.m.) and the reception at Heidelberg Town Hall (7 to 9.30 p.m.) on 3 June 2011</strong></td>
</tr>
<tr>
<td>[ ] Yes</td>
</tr>
<tr>
<td>[ ] Accompanying person</td>
</tr>
<tr>
<td><strong>I will attend the champagne reception on the Castle Gallery, the Gala Dinner in the Castles Ottheinrichsbau, and the giant fireworks, 7 to 11.30 p.m. on 4 June 2011</strong></td>
</tr>
<tr>
<td>[ ] Yes</td>
</tr>
<tr>
<td>[ ] Accompanying person</td>
</tr>
</tbody>
</table>

*Included in the costs, but necessary to be filled in for organizational reasons*

---

* For Congress Participants: Opening ceremony and reception with cold and warm buffet, participation in the conference programme during 2½ days, lunch on Friday and Saturday, coffee, beverages and snacks during morning and afternoon breaks, organ concert, reception at Town Hall and the Gala Dinner at Heidelberg Castle with giant fireworks.

** For Accompanying persons: Opening ceremony and reception with cold and warm buffet, organ concert, reception at Town Hall and the Gala Dinner at Heidelberg Castle with giant fireworks.

---

**Friday Morning Neckar Valley Roundtrip** with additional costs of € 45 per person |
| [ ] Yes | [ ] No |
| [ ] Accompanying person | [ ] Without accompanying person |

**Friday Afternoon Heidelberg City Tour** with additional costs of € 25 per person |
| [ ] Yes | [ ] No |
| [ ] Accompanying person | [ ] Without accompanying person |

**Saturday Morning Schwetzingen/Speyer** with additional costs of € 53 per person |
| [ ] Yes | [ ] No |
| [ ] Accompanying person | [ ] Without accompanying person |

**Total Amount to Be Paid** Including Conference Fees as well as Additional Excursions (You will receive a bill which has to be paid within 14 days to make registration valid.) **0.00 €**
# Abstract Submission Form

**Type of Presentation**  
(Please indicate your preference; we will do our best but please note that your preference can not be guaranteed.)
- [ ] Oral (10 min)  
- [ ] Oral (20 min)  
- [ ] Poster  
- [ ] Application for MEDI-CHEM Prize  
- [ ] Application for MEDI-CHEM Scholarship  
- [ ] Application for Young Professionals Award

**Deadline: 15 January 2011**  
To complete the Abstract Form, please refer to the instructions and to the example.

<table>
<thead>
<tr>
<th>Title</th>
<th>Presenting Author’s Family Name/Last Name/Surname</th>
<th>Prefix  (e.g. van, von, de)</th>
<th>Presenting Author’s First Name</th>
<th>Organization/Institute/Company Name</th>
<th>Title of Presentation (CAPS)</th>
<th>Author(s)</th>
<th>Institution (for each author)</th>
<th>City, Country (for each author)</th>
<th>Text of Abstract</th>
</tr>
</thead>
</table>

**Indicate your preferred Category / Subject / Topic**

- [ ] Occupational Health in a Changing World
- [ ] REACH – Impact on occupational and environmental health
- [ ] Nanotechnology – Challenges and solutions
- [ ] Strategic Approach to International Chemicals Management (SAICM) – Status and developments
- [ ] Biomarkers – Progress in research and practical application
- [ ] Toxicology – new results, emerging risks
- [ ] Regulation in occupational health – Recent developments
- [ ] Shift work and cancer – Current discussion
- [ ] Case Reports – Interesting observations in the occupational health world
- [ ] Occupational health – Trends and evolution
- [ ] Adverse effects on employees, customers and the general public – Preventive measures

The Scientific Committee will decide session and scheduling

Formally presented papers at the Congress will be published at www.medichem2011.org.

Should this Presentation be accepted by the Scientific Committee of the Congress, it will be published in the Abstract Book. Hereby I do agree with the statement above and I do give the right to publish this abstract in the Abstract Book of the Congress and my paper at www.medichem2011.org.

Name:  
Date:
Awards and Credits

MEDICHEM Prize and Scholarships

The MEDICHEM Prize will be open to trainees in the fields of Occupational Medicine, Occupational Health (including Occupational Health Nursing), Occupational and Environmental Hygiene, Occupational Safety, Toxicology and Epidemiology. Only residents of the country hosting the congress are eligible. Applicants should submit papers for oral presentation at the Congress. Information about the MEDICHEM Prize: http://www.medichem.org/congresses/prize.asp.

MEDICHEM Scholarships based on the scientific value of the submitted paper are available to individuals whose economic situation would prevent them from attending the conference to present. Such scholarships are available to a maximum of three MEDICHEM members and non-members alike, regardless of their place of residence. Information about the MEDICHEM Scholarship: http://www.medichem.org/congresses/scholarship.asp.

The Young Professionals Award is available to a maximum of six young occupational or environmental health professionals presenting their research at the Congress. Please enquire about the special set of rules which include sponsorship by a MEDICHEM member. Information about the MEDICHEM Young Professionals Program: http://www.medichem.org/congresses/young.asp.

Credits for Continuous Medical Education

The accreditation of 15 credits (points) in the category B for participants of the MEDICHEM Congress 2011 in Heidelberg has been approved from the Medical Association of Baden-Württemberg (Landesärztekammer Baden-Württemberg) for Continuous Medical Education. A certificate will be issued during the congress.

The Swiss Accreditation Authority has approved 21 credits for participants of the whole congress.
Exhibition and Sponsoring Programme for the 39th MEDICHEM Congress 2011 in Heidelberg, Germany 2 – 5th June, 2011

Organizer:
BG RCI (Berufsgenossenschaft Rohstoffe und chemische Industrie; German Social Accident Insurance Institution for the raw materials and chemical industry, formerly BG Chemie)
Kurfürsten-Anlage 62
69115 Heidelberg/Germany
c/o Dr. med. Maren Beth-Hübner
Chair of the Organizing Committee
Tel: +49 (0)6221 523 400
Fax: +49 (0)6221 523 420
E-mail: maren.beth-huebner@bgrci.de
medichem2011@bgrci.de
Web: www.medichem2011.org

Venue:
Heidelberg Marriott Hotel, Vangerowstraße 16,
69115 Heidelberg, Germany, Phone: +49 (0)6221 908-610
www.heidelberg-marriott.com

View on the Congress Venue and Exhibition Plan.
The exhibition will be located in the same room, where also the Coffee breaks and Poster presentations will take place. The breaks will be long enough for the congress participants to walk around and inform themselves about the new developments you, the exhibitors, present. Therefore, the best possible interaction with the conference participants is expected.

The Exhibition and Sponsoring Packages are described at the Registration Form for Exhibitors and Sponsors.

To discuss any question or alternative proposals for your company’s involvement please contact:
Dr. med. Maren Beth-Hübner
Chair of the Organizing Committee
Tel: +49 (0)6221 523 400
Fax: +49 (0)6221 523 420
E-mail: maren.beth-huebner@bgrci.de (quoting “Sponsorship and Exhibition” in the subject line)
medichem2011@bgrci.de (quoting “Sponsorship and Exhibition” in the subject line)
Web: www.medichem2011.com
Registration Form for Exhibitors and Sponsors (page 1)

Pls. fill out and send to Fax number +49 (0)6221 523-420 or to postal address:
Dr. Maren Beth-Hübner  |  BG RCI  |  P.O.B. 10 14 80  |  69115 Heidelberg
or scan and send it per E-Mail to: mediche2011@bgcri.de

Exhibitor's Data:

Complete company’s name

Address (street, postcode, city, country)

Phone number  Fax number

E-Mail  Homepage

Contact person (first name and family name)

Exhibitor Packages: (Pls. see exhibition map)

☐ Leaflet Package: Your flyer/advertising material placed within delegate pack.

Price: 900 €*

☐ Standard Exhibitor Package: (Area: 4 m²) including table and two chairs.
Your organisation logo advertised via the conference website, on meeting agenda (handout to all delegates), as well as on conference title slides. Two exhibitor passes (enabling access to all conference sessions, as well as refreshments at the lunch and coffee breaks).

Price: 1,800 €*

☐ Extra Exhibitor Package: (Area: 6 m²) including table and two chairs with space for a banner or poster. Your organisation logo and weblink to your website advertised via the conference website, on meeting agenda (handout to all delegates), as well as on conference title slides. Two extra exhibitor passes (enabling access to all conference sessions, as well as refreshments at the lunch and coffee breaks and additionally, access to all social events, like welcome reception, organ concert and reception at Heidelberg Town Hall, as well as Reception and Gala Dinner with Giant Fireworks at Heidelberg Castle).

Price: 2,400 €*

Booth areas will be allocated according to registration entry!

* Pls. note that booking an exhibition booth includes standard electrical supply (220 V) with three sockets, which will be invoiced with a flat rate of 100 €.

Booth Information:

We will be showing the following products/ services: __________________________________________

Conditions, Policies und General Information:

All prices include VAT. The entire stand rental is due within 10 days of date of invoice. With this registration the conditions of participation of the MEDICHEM Congress 2011 are legally binding accepted.

Date, place  Company stamp, signature
Sponsor's Data:

<table>
<thead>
<tr>
<th>Complete company's name</th>
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<table>
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<tr>
<th>Address (street, postcode, city, country)</th>
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<tr>
<th>Phone number</th>
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<th>E-Mail</th>
<th>Homepage</th>
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</table>

Contact person (first name and surname)

<table>
<thead>
<tr>
<th>Sponsoring Packages: (Pls. see exhibition map)</th>
</tr>
</thead>
<tbody>
<tr>
<td>➕ DIAMOND-Package: (over 10,000 €, on appointment)</td>
</tr>
<tr>
<td>➕ PLATINUM-Package: (10,000 €)</td>
</tr>
<tr>
<td>➕ GOLD-Package: (4,000 €)</td>
</tr>
<tr>
<td>➕ SILVER-Package: (2,000 €)</td>
</tr>
<tr>
<td>➕ BRONZE-Package: (1,000 €)</td>
</tr>
<tr>
<td>➕ CONTRIBUTOR-Package: (over 500 €)</td>
</tr>
</tbody>
</table>

The right of DIAMOND and PLATINUM Sponsorships:
- Visualization of the company in Congress promotional documents (Web, Program, Abstract Book).
- Logo and List of Sponsors by categories in Congress Programme (Web Link and contact address).
- A free exhibition booth (double for „Diamond Sponsors“).
- An advertisement in the Programme Book in a relevant position.
- Free registration of two persons.
- An announcement inside the Congress bag.
- Two tickets for Congress dinner.
- Discounts in sponsorship opportunities.

The right of GOLD, SILVER and BRONZE Sponsorships:
- List of Supporters by categories in Congress Programme (paper + electronic).
- An advertisement in the Programme Book (Gold only).
- Free registration of one person (Gold and Silver only).
- One ticket for Congress dinner (Gold and Silver only).
- Discount for an advertisement in Congress Programme Book (40/30/20%).
- Discount for an announcement inside the Congress bag at (40/30/20%).
- Discounts in other sponsorship opportunities (Gold).

The right of CONTRIBUTOR Sponsorship:
- List of Contributors in Congress Programme (paper + electronic)
Specific Sponsorship Opportunities:

We offer to be a sponsor for SOCIAL EVENTS and CATERING:

- Welcome Reception with cold and warm buffet/Open Ceremony, 2 June 2011 7,000 Euro
- Brass music/Open Ceremony, 2 June 2011 1,000 Euro
- Organ concert and rent of the Church of the Holy Spirit, 3 June 2011 750 Euro
- Reception/Heidelberg Castle Gallery, 4 June 2011 3,000 Euro
- Gala Dinner/Heidelberg Castle, including giant fireworks, 5 June 2011 20,000 Euro
- Music/Gala Dinner 1,000 Euro

During Conference:

- Lunch and all Coffee Breaks on Friday, 3 June 2011 8,820 Euro
- Lunch and all Coffee Breaks on Saturday, 4 June 2011 8,820 Euro
- Lunch and all Coffee Breaks on Sunday, 5 June 2011 7,420 Euro

We offer to be a sponsor for PRINTED MATERIAL:

- Nameplate 300 Euro
- Final conference programme 2,000 Euro
- USB Memory (pendrive) with abstracts and programme 3,000 Euro
- Advertisement (inner page) final programme 1,000 Euro
- Advertisement (cover page) final programme 2,500 Euro
- Simple Announcement inside the congress bag (a 2-A4 sheets, diptic, triptic brochure) (free for next Organizers of the MEDICHEM Congress 2012) 1,000 Euro
- Big Announcement insert inside the bag (up to 16 pages brochure) 2,000 Euro
- Congress bag (including pen and note paper) 3,000 Euro

Partial sponsorship may be accepted.

We offer to be a sponsor for INVITED SPEAKERS:

- Speaker Sponsorship: 2,000 Euro
  - Mention of your company on the corresponding page in the main programme
  - Mention on the programme page of the MEDICHEM 2011 Congress Website
  - Display of a flyer in the conference bag/Congress Website

Sponsorship Entitlements include:

ALL CASES: Logo on sponsor's list in Program and Congress website as well as weblink to the sponsors website.
SOCIAL EVENTS Banner informing that the welcome cocktail or the gala dinner has been full/partly offered by ....
CATERING Banner informing that the Coffee break and lunch has been full/partly offered by ....
PRINTED MATERIAL Company Logo and gratitude's in the printed material.

To discuss any question or alternative proposals for your company's involvement please contact:
Dr. med. Maren Beth-Hübner, Chair of the Organizing Committee, Tel: +49 (0) 6221 523 400 E-mail: maren.beth-huebner@bgrci.de

Conditions, Policies und General Information:

All prices include VAT. With this registration the conditions of participation of the MEDICHEM Congress 2011 are legally binding accepted.
Dear Colleague,

In the name of our Organizing Committee we warmly invite you to participate at the 2011 International Occupational Health Event - Medichem 2011 in Heidelberg! With an A-List of brilliant speakers we intend to provide scientific excellence - hopefully enriched by your contribution!

Exchange of knowledge on cutting-edge developments between science and practice within the different topics of the MEDICHEM 2011 Theme: Occupational Health in a Changing World - this is what we will be offering you from 2 - 5 June 2011.

Please visit our website, register early and send in your abstract!

Thomas Köhler, Dr. Maren Beth-Hübner, Prof. Dr. Alfred Thiess

In addition, it is our goal - and we personally will put all our best efforts into achieving it - that all participants, including the exhibitors and sponsors, will not only benefit from a productive and profitable congress but also enjoy a few memorable days in Heidelberg in the early summer of 2011.

For our retired colleagues we offer a reduced fee. Register now for reduced prices!

In pursuit of this goal we offer an all-inclusive conference package and an attractive social programme as well as a comfortable congress venue with on-site accommodation, situated on the banks of the Neckar River, in our famous old and romantic University City of Heidelberg, Germany.

We are certain this information will have kindled your interest in attending this major event.

We are greatly looking forward to welcoming you personally at the 39th MEDICHEM-Congress 2011 in Heidelberg, Germany for an unconventional as well as socially enjoyable meeting.

Heidelberg, October 25th, 2010

Thomas Köhler
(Managing Director BG RCI)

Dr. med. Maren Beth-Hübner
(Chair of the Organizing Committee MEDICHEM 2011)

Prof. Dr. med. Alfred Thiess
(Founder & Honorary President of MEDICHEM)

You're receiving this email because you are either a MEDICHEM-Member or the chair of the congress, Dr. Maren Beth-Huebner, BG RCI, Heidelberg, Germany, thought you might be interested to attend the MEDICHEM 2011 Congress.

To unsubscribe from her list of potentially interested persons, please click here (medichem2011@bgrci.de).
Dear Colleague,

The deadline for early registration is March 15, 2011. Register early for reduced prices! Visit our [website](http://www.medichem2011.org) and view the all-inclusive conference package. Look at the [program](http://www.medichem2011.org) (preliminary) of the 39th International MEDI-CHEM Congress on Occupational and Environmental Health in the Production and Use of Chemicals: "Occupational Health in a Changing World". **Come to Heidelberg, Germany, from 2 - 5 June 2011!** [Complete the Registration Form](http://www.medichem2011.org) and send to [medichem2011@bgrci.de](mailto:medichem2011@bgrci.de).

Thomas Köhler  
(Managing Director BG RCI)

Dr. med. Maren Beth-Hübner  
(Chair of the Organizing Committee MEDICHEM 2011)

Prof. Dr. med. Alfred Thiess  
(Founder & Honorary President of MEDI-CHEM)

You're receiving this email because you are either a MEDICHEM-Member or the chair of the congress, Dr. Maren Beth-Huebner, BG RCI, Heidelberg, Germany, thought you might be interested to attend the MEDICHEM 2011 Congress.

To unsubscribe from her list of potentially interested persons, please [click here](mailto:medichem2011@bgrci.de).
Dear Exhibitor, dear Sponsor,
I'm proud to invite you today to participate actively at the international MEDICHEM Congress from 2 - 5 June 2011 in Heidelberg!

It is anticipated that the 2011 International Occupational Health Event - MEDICHEM 2011 in Heidelberg - will attract around 200 top delegates from all over the world: Occupational health physicians, especially the medical directors of the global chemical and pharmacological players, occupational hygienists, epidemiologists, toxicologists, environmental and safety specialists, occupational health nurses, regulators, and students in these fields.

With an A-List of brilliant speakers we intend to provide scientific excellence and exchange of knowledge on cutting-edge developments between science and practice within the different topics of the MEDICHEM 2011 Theme: Occupational Health in a Changing World:

- **REACH** - Impact on occupational and environmental health
- **Nanotechnology** - Challenges and solutions
- **Strategic Approach to International Chemicals Management (SAICM)** - Status and developments
- **Biomarkers** - Progress in research and practical application
- **Toxicology** - New results, emerging risks
- **Regulation** in occupational health - Recent developments
- **Shift work and cancer** - Current discussion
- **Case Reports** - Interesting observations in the occupational health world
- **Occupational health** - Trends and evolution
- **Adverse effects on employees, customers and the general public** - Preventive measures

We will stage a congress touching all areas and aspects of preventive occupational health and safety. Besides this it is my goal - and I personally will put all my efforts into it - that all participants, including the exhibitors and sponsors, will not only benefit from a productive and profitable congress but also enjoy a few memorable days in Heidelberg in the early summer of 2011. To reach this goal we offer an all-inclusive conference package and an attractive social programme as well as a comfortable congress venue with on-site accommodation, situated on the banks of the Neckar River. The City of Heidelberg, with its romantic townscape is an event in itself and attracts millions of visitors from all over the world.

Therefore MEDICHEM 2011 is presenting an excellent advertising opportunity for agencies, companies and organisations which have to do something with the themes and topics of the congress and which want to reach the target groups of the conference.

Exhibition will be posed in the same area of the breaks, which will be long enough for the congress participants to walk around and inform themselves about the new developments you, the exhibitors, present. Below are examples of some of the exhibition and sponsoring packages available, although we are happy to be flexible to reflect each organisation's individual needs. To discuss further your company’s involvement in
Sponsorship and Exhibition at MEDICHEM 2011, please contact Dr. Maren Beth-Hübner, medichem2011@bgrci.de, quoting "Sponsorship & Exhibition" in the subject line.

With this information I am sure to have kindled your interest in attending this major event.

I am greatly looking forward to welcoming you personally at the 39th MEDICHEM-Congress 2011 in Heidelberg, Germany for an unconventional as well as socially enjoyable meeting!

Dr. med. Maren Beth-Hübner
(Chair of the Organizing Committee MEDICHEM 2011)
Heidelberg, March 15, 2011

Exhibition and Sponsorship Programme for the 39th MEDICHEM Congress 2011 in Heidelberg, Germany, 2 - 5 June, 2011

To unsubscribe from the list of potentially interested Exhibitors and/or Sponsors, please click here (medichem2011@bgrci.de).
Dear Colleague,

The first draft of the comprehensive Scientific Program of the 39th International MEDICHEM Congress on Occupational and Environmental Health in the Production and Use of Chemicals: "Occupational Health in a Changing World" from 2 - 5 June 2011 in Heidelberg, Germany, is available. Please have a look at www.medichem2011.org or in the attachment.

The deadline for registration of the optional excursion to the cradle of MEDICHEM, Ludwigshafen, by invitation of the BASF SE is April 15.

Also the deadline for booking of the congress hotel at the special rate via our congress website is April 15.

Please find the Registration Form attached for further information and have a look at the website www.medichem2011.org.

Come to Heidelberg, Germany, from 2 - 5 June 2011! Complete the Registration Form (see attached) and send to medichem2011@bgrci.de.

We are greatly looking forward to welcoming you in the world famous old university town, Heidelberg.

Maren Beth-Huebner

(Chair of the Organizing and of the Scientific Committee of MEDICHEM 2011)

Dr. med. Maren Beth-Huebner
BG RCI (Berufsgenossenschaft Rohstoffe und chemische Industrie (German Social Accident Insurance Institution for the Raw Materials and Chemical Industry, formerly BG Chemie))
Kurfuersten-Anlage 62
69115 Heidelberg
Telefon: 0049 6221 523-400
Fax: 0049 6221 523-420
E-Mail: maren.beth-huebner@bgrci.de
Internet: http://www.bgrci.de
Dear (potential) Exhibitor,

My last warm invitation to participate at the 39th International MEDICHEM Congress "Occupational Health in a Changing World" from 2 - 5 June 2011 in Heidelberg, Germany, as an exhibitor is reaching you.

The deadline for registration is May 10!

There is still some space left for you. Come to Heidelberg, Germany, from 2 - 5 June 2011! Complete the Registration Form (see attached) and send to medichem2011@bgrci.de.

Please feel free to contact me to clarify your questions and to discuss our offers.

For further information please have a look at www.medichem2011.org.

I am looking forward to hearing from you.

Best regards,

Maren Beth-Huebner

(Chair of the Organizing and of the Scientific Committee of MEDICHEM 2011)

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Dr. med. Maren Beth-Huebner
BG RCI (Berufsgenossenschaft Rohstoffe und chemische Industrie (German Social Accident Insurance Institution for the Raw Materials and Chemical Industry, formerly BG Chemie))
Kurfuersten-Anlage 62
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Last chance to register until May 15! (April 29, 2011)

Dear Colleague,

My last warm invitation to participate at the 39th International MEDICHEM Congress "Occupational Health in a Changing World" from 2 - 5 June 2011 in Heidelberg, Germany, is reaching you.

The deadline for registration is May 15.

Please have a look at www.medichem2011.org or in the attachment.

There are still some rooms left at the congress hotel, the Heidelberg Marriott, at the special rate via our congress website.

Come to Heidelberg, Germany, from 2 - 5 June 2011! Complete the Registration Form (see attached) and send to medichem2011@bgrci.de.

I personally will put all my efforts into it, and my team will support me with all its strength, that all participants will not only benefit from a productive and profitable congress but will also enjoy a few memorable days in Heidelberg in the early summer of 2011.

Maren Beth-Huebner

(Chair of the Organizing and of the Scientific Committee of MEDICHEM 2011)

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Dr. William Murray Coombs

Prof. Dr. Ken Donaldson

Dr. Andreas Flückiger

Prof. Dr. Heidi Foth
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3. Gabriele Haass
4. Prof. Dr. Andrea Hartwig
5. Prof. Dr. Uwe Heinrich
6. Dr. Steffen Hitzeroth
7. Dr. Heiko U. Käfferlein
8. Dr. Matthias Kluckert
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* passed away
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