

# Novel Approaches to Safety Evaluation & Risk Assessment



**18-19 January 2011**  
**Venue: Cranage Hall, Cheshire**

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This conference will spotlight the human hazard database that underpins safety evaluation and discuss novel approaches to risk assessment. The theme is broadly based on the European REACH and Plant Protection product legislation and will cover both basic and regulatory science. The sessions are designed to be interactive and each will conclude with the opportunity for the floor and the speakers to discuss the topics arising from the presentations and to share experiences. Presentations will include learning from recent submissions using information from *in vitro* and human studies with a scientific focus on non-genotoxic carcinogenesis and endocrine disruption.

# Summary Timetable

## Day 1 (18 January 2011)

Arrive approx 1.00 pm for coffee

Opening Remarks 1.45 pm – Dr Cliff Elcombe and Dr Mac Provan

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### Session 1 – Regulatory context 2.00–3.30 pm

Chair: David Farrar OBE, Ineos Chlor Ltd

- Dr David Owen, Shell - The REACH 2010 Milestone: Experiences and Expectations
- Charlotte Croudace, RSA - Impacts and Challenges Encountered in the Introduction of the EU CLP Regulation
- Dr Paul Parsons, Syngenta - Are Data Rich Compounds More Hazardous?
- Panel discussion

Break for coffee 3.30–4.00 pm

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### Session 2 – Non-genotoxic carcinogenicity

4.00–5.30 pm

Chair: Dr Cliff Elcombe, CXR Biosciences

- Prof Brian G. Lake, LFR Molecular Sciences - Rodent Liver Carcinogenesis by Non-Genotoxic CYP2B and CYP4A Inducers: Modes of Action and Human Relevance
- Dr Terry Orton, Liverpool University - Hepatocyte Proliferation a Key Mechanism of Action Event in Hepatocarcinogenesis Induced by Non-genotoxic Compounds
- Dr Cliff Elcombe, CXR Biosciences - The Use of Nuclear Receptor Knockout and Humanised Mouse Models in the Risk Assessment of Non-genotoxic Hepatocarcinogens
- Panel discussion

### Conference Dinner

Drinks reception 7.00 pm, followed by dinner 7.30 pm. After dinner speaker: Prof John Foster.

## Day 2 (19 January 2011)

Session 3 – Data gaps within the context of REACH and expert judgements 9.00–10.30 am

Chair: Prof Jon Heylings, Keele University / Prof Ian Kimber, Manchester University

- Dr Barry Elliott / Dr Mac Provan, RSA - A Weight of Evidence Approach
- Prof Ian Kimber, University of Manchester - Skin Sensitisation: Hazard Identification and Characterization and Interpretive Challenges
- Prof Jon Heylings, Keele University - *in vitro* Approaches for the Assessment of Dermal Absorption of Chemicals From Their Formulated Products
- Panel discussion

Break for coffee 10.30–11.00 am

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### Session 4 – Endocrine disruption 11.00 am–12.50 pm

Chair: Dr Remi Bars, Bayer

- Dr Jenny Odum, RSA - Assessing Endocrine Disruption and its Relevance to Human Health
- Prof Tom Hutchinson, CEFAS - Endocrine Disruption in Aquatic Organisms: OECD Test Guidelines & Applications in Risk Assessment
- Dr Remi Bars, Bayer S.A.S. - Dose Response and Threshold in Endocrine Disruption
- Dr Simon M Plummer, CXR - Effects of Chemicals on Gene Expression and Dysgenesis in Fetal Rat Testis, From Molecular Mechanism to Predictive Screen

Break for lunch 12.50–1.45 pm

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### Final discussion session 1.45–2.30 pm

Chair: Dr Sue Hubbard, Rio Tinto

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Close of meeting 2.30 pm

# Full Programme

## Day 1 (18 January 2011)

Arrive approx 1.00 pm for coffee

Opening Remarks 1.45 pm – Dr Cliff Elcombe and Dr Mac Provan

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### Session 1 – Regulatory context 2.00–3.30 pm

REACH regulation and changes to the Plant Protection Product Directive require industry to address new and sometimes complex areas of potential human hazard and risk assessment of substances and mixtures. For REACH, many of these substances are 'data poor' against the requirements and conclusions on hazard (key endpoints for risk assessment and for classification) may be made without resorting to additional animal testing. In relation to derived no effect level (DNEL) proposals, reference to established occupational exposure levels, be it at European or National level, versus establishing DNELs de novo needs to be considered. In the latter case, identification of critical effects/endpoints for human risk assessment, derived from animal and/or human data, and the application of appropriate assessment factors is critical. Focus of endpoints previously not addressed for regulatory compliance such as the potential for endocrine disruption also add new challenges.

**Chair: David Farrar OBE, Ineos Chlor Ltd**

**Dr David Owen, Shell – The REACH 2010 Milestone: Experiences and Expectations**

- REACH infrastructure
- Practicalities on preparing chemical safety assessments
- Post-registration activities
- Legislation infrastructure: authorisation; revision; global uptake

**Charlotte Croudace, Director of Regulatory Affairs, RSA – Impacts and Challenges Encountered in the Introduction of the EU CLP Regulation**

- Changes in classification criteria between DSD and CLP
- Classification criteria/'cut-offs' under REACH and revised PPP and BPD
- C&L Inventory & harmonisation process including transition period and current Registry of Intentions with PPP and BP products.
- Downstream hazard communication (eSDSs)

**Dr Paul Parsons, Principal Toxicologist, Global Toxicology & Health Science, Syngenta – Are Data Rich Compounds More Hazardous?**

- Test guideline philosophy; is the focus on detecting hazard or evaluating risk?
- Does evaluating carcinogenic potential at limit doses make any sense?
- The ever-growing mammalian toxicology database; a precautionary tale
- The science moves-on; adversity, mode of action and human relevance

**Panel discussion**

**Break for coffee 3.30–4.00 pm**

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## Session 2 – Non-genotoxic carcinogenicity 4.00–5.30 pm

This session will provide an opportunity to review the mechanisms of non-genotoxic carcinogenicity (NGC) in the liver and consider the Mode of Action framework for human relevance. Conventional models, such as rodents and hepatocytes, currently used to investigate NGC will be assessed. Finally, the use of novel models such as the knockout and humanised nuclear hormone receptor (NHR) mice e.g. PXR and CAR will be discussed in the context of their use in risk assessment.

**Chair: Dr Cliff Elcombe, CXR Biosciences**

### **Prof Brian G. Lake, LFR Molecular Sciences – Rodent Liver Carcinogenesis by Non-Genotoxic CYP2B and CYP4A Inducers: Modes of Action and Human Relevance**

- Rodent liver tumour formation by constitutive androstane receptor (CAR) activators (CYP2B inducers) and peroxisome proliferator activated-receptor alpha agonists (CYP4A inducers)
- Effects in rodent liver
- Species differences in response
- IPCS/ILSI mode of action (MOA) framework
- Human relevance

### **Dr Terry Orton, Honorary Lecturer, Liverpool University – Hepatocyte Proliferation a Key Mechanism of Action Event in Hepatocarcinogenesis Induced by Non-genotoxic Compounds**

- Relationship between liver growth (hyperplasia and hypertrophy) and liver tumour formation in rodents
- How hepatocyte proliferation is determined *in vitro* and *in vivo*
- A matrix for assessment of hepatocyte proliferation as a risk factor in man
- Examples of differing hepatocyte proliferation response in laboratory species versus man

### **Dr Cliff Elcombe, CXR Biosciences – The Use of Nuclear Receptor Knockout and Humanised Mouse Models in the Risk Assessment of Non-genotoxic Hepatocarcinogens**

- Introduction to knockout and humanised mice.
- Characterisation of "TransADMET" mice.
- Nuclear receptor knockout mice and humanised mouse models to investigate nongenotoxic hepatocarcinogenesis.
- Potential role in hazard and risk assessment.

## **Panel discussion**

Conference Dinner

Drinks reception 7.00 pm

Dinner 7.30 pm

After dinner speaker: Prof John Foster

## Day 2 (19 January 2011)

### Session 3 – Data gaps within the context of REACH and expert judgements.

9.00–10.30 am

For substances that do not have all the required guideline studies to meet REACH requirements a waiver is applicable on the basis that further work is not scientifically justified if there is sufficient weight of evidence to define a robust conclusion. For many endpoints, that weight of evidence conclusion may be heavily influenced by, for example, non-guideline study types (*in vitro* or *in vivo*) and/or predictions made from validated tools such as OECD toolbox, or indeed by direct read-across to study results from similar areas of chemistry. In practice, expert judgements are used to combine the available datasets to provide a robust weight of evidence argumentation for each endpoint. Typically, molecular similarity of the read-across candidate(s) and their toxicokinetic behaviour may be considered in conjunction with expert assessment of the potential hazard for the endpoint of concern, for example genetic toxicity, sensitisation etc. Clearly for some systemic toxicity endpoints read-across to *in vivo* studies of related substances/metabolites is invaluable. Such expert examination of a database may also highlight where, for example, a simple cost-effective *in vitro* study, or careful evaluation of complex data from human volunteer studies, may render a significantly different DNEL for the substance in question. This session will explore the roles of expertise and toolkits to address data gaps.

**Chair: Prof Ian Kimber, Manchester University**

**Dr Barry Elliott, Senior Toxicologist, RSA / Dr Mac Provan, Director, RSA – A Weight of Evidence Approach**

- Uncertainties in human health information may be assessed by consideration of the overall evidence available
- Read-across to similar chemistry and/or (Q)SAR information can be helpful surrogates within a Weight of Evidence approach
- Overall, the information needs to be adequate for classification and labelling and/or risk assessment
- Expert judgement is required to 'weight' the value of the individual pieces of information and determine if there is sufficient evidence to conclude on an endpoint
- Weight of Evidence approach is well-established for some toxicological assessments, REACH defines new guidelines for documentation

**Prof Ian Kimber, University of Manchester – Skin sensitisation: Hazard Identification and Characterization and Interpretive Challenges**

- Principles of skin sensitisation
- Local lymph node assay and hazard identification
- LLNA and hazard characterisation
- Challenging results and interpretations

**Prof Jon Heylings, School of Pharmacy, Keele University – *In vitro* approaches for the assessment of dermal absorption of chemicals from their formulated products**

- OECD, EFSA and SCCS guidance
- Human skin models
- Skin bound residues
- Read-across between formulations

**Panel discussion**

**Break for coffee 10.30–11.00 am**



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## Session 4 – Endocrine disruption 11.00 am–12.50 pm

The assessment of chemicals for their potential to cause endocrine disruption in both humans and wildlife populations is a requirement of the REACH legislation and of the new Plant Protection Directive in Europe. The criteria for defining a chemical as an endocrine disruptor, however, are not yet agreed, but there are a number of initiatives within Europe where criteria are being proposed. These are also largely based on the Mode of Action framework for human relevance. This session will focus on current regulatory requirements, developments in testing for endocrine disruptors and new science within the field.

### Chair: Dr Remi Bars, Bayer SAS

#### **Dr Jenny Odum, Senior Toxicologist, RSA – Assessing Endocrine Disruption and its Relevance to Human Health**

- Regulatory requirements for assessing endocrine disruption
- Testing strategies for effects on human health
- Toxicological endpoints and hazard determination
- Case study examples

#### **Prof Tom Hutchinson, Programme Scientist, Environment & Health, Centre for Environment Fisheries & Aquaculture Science – Endocrine Disruption in Aquatic Organisms: OECD Test Guidelines & Applications in Risk Assessment**

- Brief overview on key aquatic studies that have influenced policy requirements for endocrine disrupter assessment
- Update on the OECD framework on test guideline development using fish, invertebrates & amphibians
- Environmental risk assessment case studies where endocrine alerts have been a key driver
- Beyond reproductive endocrinology into mode-of-action ecotoxicology
- Developing policy frameworks and the need for intelligent testing strategies including endocrine active chemicals

#### **Dr Remi Bars, Group Leader Research Toxicology, Bayer S.A.S. – Dose Response and Threshold in Endocrine Disruption**

- Concept of threshold in toxicology
- Modes of action in endocrine toxicity
- Dose response using *in vitro* and *in vivo* endpoints
- Case study examples

#### **Dr Simon M Plummer, CXR Biosciences – Effects of Chemicals on Gene Expression and Dysgenesis in Fetal Rat Testis, From Molecular Mechanism to Predictive Screen**

- Mechanism of testicular dysgenesis induced by certain phthalate esters in rats exposed in utero
- The use of Laser Capture Microdissection, cDNA microarrays and ChIP-on-chip analysis to elucidate receptor-mediated mechanisms
- Mechanism-based *in vivo* short term screen for potential effectors of dysgenesis

### Panel discussion

Break for lunch 12.50–1.45 pm



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## Final discussion session 1.45–2.30 pm

Discussion aimed at identifying issues and learning from the previous sessions, particularly related to the first submission deadlines under REACH.

**Chair: Dr Sue Hubbard, Principal Adviser – Product Toxicology, Rio Tinto**

Close of meeting 2.30 pm



# Speaker and Chair Biographies

## **David G Farrar OBE , Ineos Chlor Ltd**

David Farrar is the Toxicology Manager for Ineos Chlor Ltd and is based in Runcorn.

A graduate in Pharmacy at the University of Bradford, with Special Honours in Pharmacology, David spent seven years in the pharmaceutical industry as a research pharmacologist. He was recruited by ICI in 1977 into its Central Toxicology Laboratory as an inhalation toxicologist and spent his first three years with the company seconded to the Flammability Research Center, University of Utah, Salt Lake City, USA.

David moved into the ICI (now Ineos Chlor) occupational health function at Runcorn in 1987. He contributes to the activities of several CEFIC Sector Groups and is a member of the ECETOC Scientific Committee.

David has worked on several regulatory committees at EU and national level and is an independent member of the UK HSE WATCH Committee. He has published several papers on different aspects of occupational and industrial toxicology and health risk assessment and is a Fellow of the British Toxicological Society. In 2004, he was awarded an OBE in the Queen's Birthday Honours list for his services to occupational health.

## **Dr David Owen, Shell**

David Owen joined Shell Research after gaining his PhD from Southampton in 1975. He is currently a senior principle scientific advisor in Shell Chemicals, coordinating global strategy for major health, environmental and regulatory issues. David has first-hand experience of experimental toxicology and product regulatory processes. He has worked with a range of Europe, and US trade association product groups. He currently participates in several inter-industries and academic groups including the European chemicals federation, Cefic, where he sits on teams coordinating REACH, the Long range Research Initiative (LRI) and Emerging Issues and Policy and Innovation. David is a member of the Scientific Committee of ECETOC, and is on a number of advisory committees, including Johns Hopkins University's Centre for Alternatives to Animal Testing (CAAT). One of his most recent challenges has been to implement REACH across Shell companies, the first milestone being the completion of several hundred registrations during 2010.

## **Charlotte Croudace, Director of Regulatory Affairs, Regulatory Science Associates**

Charlotte worked in the chemical industry for 14 years at Brixham Environmental Laboratory and then as an agrochemical regulatory manager for Zeneca and Syngenta in the UK and Switzerland. Charlotte broadened her skill base further during her 4 years as a Senior Associate with an established consultancy company, toXcel. In May 2007 she co-founded RSA.

As an experienced project manager and regulatory scientist, Charlotte's expertise includes an in-depth understanding of the dossier requirements for general chemicals under REACH as well as for agrochemical and biocide registration and re-registration in the EU. She also has practical experience in substance and product hazard classification and labelling under DSD/DPD and the new CLP regulation.

### **Dr Paul Parsons, Principal Toxicologist, Global Toxicology & Health Science, Syngenta UK Ltd**

Dr Paul Parsons is a regulatory toxicologist with over 16 years experience of working both in industry and government (UK, HSE). Paul has extensive experience with chemicals regulation in Europe and also in the regulation of agrochemicals in the USA. Currently employed as a Principal Toxicologist with Syngenta UK Ltd, the focus of Paul's experience over the last 7 years has been in the development and registration of new pesticide active ingredients spanning a range of activities from lead finding to full regulatory development programs. In addition to data generation, Paul has extensive experience in downstream use of toxicology data in human health risk assessment and classification and labelling. In recent years, Paul has been involved in a number of activities focused on developing the underlying science and regulatory frameworks for the application of risk assessment methodologies including cumulative risk assessment.

### **Dr Barry Elliott, Senior Toxicologist, Regulatory Science Associates**

Barry Elliott has more than 30 years of experience in toxicology ranging from investigative toxicology to project management. His core discipline spanning this time has been genetic toxicology and Barry is a recognised expert in this field, with membership of expert Committees and also past appointments as President of the UKEMS and Secretary of the EEMS. He has an interest and expertise in chemical structure activity relationships in genetic toxicology and carcinogenesis. He joined ICI following his PhD and has held positions with this company and through subsequent mergers to the current Syngenta, including Head of Genetic Toxicology, Head of Metabolism and Genetic Toxicology and Senior Toxicologist responsible for all toxicology areas of a portfolio of leading agrochemical products. Barry has prepared and presented positions on chemicals to regulatory agencies around the world. During his time in ICI and also latterly in Syngenta through its contract research business, Barry has been involved with chemicals in the Industrial, Pharmaceutical and Agrochemical sectors.

### **Dr Mac Provan, Director, Regulatory Science Associates**

Co-founder of RSA, Mac has over 30 years' experience in chemistry, biochemistry and toxicology with major companies (ICI, Zeneca and Syngenta) and was an investigative toxicologist at the world-famous Central Toxicology Laboratory (CTL) from 1979 to 2003. He is a recognised expert in the investigation and understanding of the role of metabolism and kinetics in species-specific responses to xenobiotics and has made numerous contributions in this field of regulatory science. In addition to these key scientific skills, Mac also has significant experience of project management and information systems management. He was responsible for development of appropriate in-house 'decision-making' safety information for potential new products, prior to defining and managing the development of safety data packages and science-based registration strategy for new product registration and/or defence. More recently Mac has been involved in REACH technical dossier compilation and project management, particularly for substances with complex toxicology issues.

### **Professor Ian Kimber, University of Manchester, UK**

Ian Kimber is currently Professor of Toxicology and Associate Dean for Business Development in the Faculty of Life Sciences at the University of Manchester. Previous to that he was Head of Research and Principal Fellow at the Syngenta Central Toxicology Laboratory.

He has broad research interests based around immunotoxicology, including: (a) the characteristics of allergy caused by chemical, drugs and proteins, (b) cutaneous immune responses and the roles played by Langerhans cells (c) functional subpopulations of T lymphocytes and (d) the development and evaluation of novel approaches to safety assessment.

Professor Kimber holds, and has held, a variety of positions on national and international expert and scientific advisory committees. Currently these include the following: UK Medical Research Council (MRC) Training and Career Group, Special Advisor to the MRC on Industrial Liaison, UK Medicines and Healthcare products Regulatory Agency (MHRA) Committee for Safety of Devices, Programme Advisor Food Standards Agency Food Allergy and Intolerance Research Programme, member of the Executive Committee of the MRC Centre for Drug Safety Sciences. He is also Chair of the UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs).

He has published over 500 research papers, review articles and book chapters and serves currently on the editorial boards of toxicology, immunology, dermatology and pathology journals.

Professor Kimber has received a number of awards and prizes. These include: the SmithKline Beecham Laboratory Animal Welfare Prize (2000) (jointly with David Basketter and Frank Gerberick), the 9th Robert A Scala Award in Toxicology (2001), the Doerenkamp-Zbinden Foundation Prize for Realistic Animal Protection in Biomedical Research (2001), Society of Toxicology Enhancement of Animal Welfare Award (2003) (jointly with Frank Gerberick), and Society of Toxicology Immunotoxicology Career Achievement Award (2005). In 2002 he was invited to present the fourth FRAME Annual Lecture: Reduction, Refinement, Replacement: Putting the Immune System to Work. In 2010 Professor Kimber received the Bo Holmstedt Memorial Fellowship Award and Lecture at the International Congress of Toxicology.

### **Professor Jon Heylings, School of Pharmacy, Keele University, UK**

Jon Heylings has spent most of his career in industry, following his BSc (Medical Sciences) and PhD (Pharmacology). He joined ICI Pharmaceuticals Division in 1979, working in Gastrointestinal Research at Alderley Park, before spending two years in the Department of Gastroenterology at the University of Texas Health Science Center in Dallas, Texas. In 1986, Jon set up a GI Research Group in Biochemical Toxicology at ICI Central Toxicology Laboratory with his work mainly focused on paraquat. Jon also developed the Dermal Absorption capabilities of CTL and was appointed Senior Toxicologist in 1999. In 2007, following the closure of CTL, Jon co-founded the Dermal Technology Laboratory (DTL Ltd) at Keele University Science Park, where he is Chairman and Chief Scientific Officer. He is also Honorary Professor of Toxicology in the Faculty of Health at the University.

### **Dr Clifford R. Elcombe, CXR Biosciences Ltd, Dundee, UK**

Dr Cliff Elcombe is co-founder and research director of CXR Biosciences Ltd. He is also a Senior Lecturer in the Biomedical Research Institute, Ninewells Hospital and Medical School, University of Dundee. He joined the University of Dundee in 1997 after an 18-year career at Zeneca's (formerly ICI) Central Toxicology Laboratory where he was a Senior Scientist in Investigative Toxicology. Dr. Elcombe received his BSc and PhD in biochemistry from the University of Surrey. He received a Royal Society travelling fellowship award to post-doc in Germany and then was appointed an Assistant Professor at the Medical College of Wisconsin.

Dr. Elcombe's research interests are focussed on understanding mechanisms of target organ toxicity thereby facilitating scientifically based risk assessment. He has long standing research interests in species differences and non-genotoxic carcinogenicity.

Dr Elcombe is the author or co-author of over 100 peer-reviewed publications and has served on several national and international advisory committees including the UK Advisory Committee on Pesticides and the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment.

### **Professor Brian G. Lake, LFR Molecular Sciences**

Brian G. Lake has PhD and DSc degrees from the University of Surrey and holds the position of Visiting Professor in the Faculty of Health and Medical Sciences. He is a Fellow of the British Toxicology Society. Brian Lake worked at BIBRA International for over 30 years and is currently head of LFR Molecular Sciences. During his career he has been involved in a wide range of multi-disciplinary research and contract projects. His research interests include xenobiotic metabolism, the induction of xenobiotic metabolising enzymes, the development of *in vitro* systems for predicting xenobiotic metabolism and toxicity; modes of action (MOAs) of non-genotoxic carcinogenesis and the extrapolation of animal data to human hazard assessment. He has published over 230 scientific papers, acted as a consultant to various international companies and is currently a member of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). Brian Lake's group at LFR perform a range of both fully GLP compliant and non regulatory laboratory studies and consultancy services for pharma, agrochemical and other clients.

### **Dr Terry Orton, Honorary Lecturer in Molecular Toxicology, Department of Pharmacology and Therapeutics, School of Biomedical Sciences, Liverpool University, UK**

Terry Orton worked at ICI Pharmaceuticals, Zeneca Pharmaceuticals and finally AstraZeneca from 1974 until retirement in 2008. During that time, he has been Head of Genetic and Experimental Toxicology and latterly Head of Molecular Toxicology within the Department of Safety Assessment. He has wide experience in exploring the mechanisms of toxicology (target organ accumulation, reactive metabolite formation and tissue binding, nongenotoxic carcinogenesis) associated with pharmaceuticals.

### **Dr Remi Bars, Group Leader Research Toxicology, Bayer S.A.S.**

Remi Bars studied pharmacy and toxicology at the University of Paris XI. He then did a PhD and a post-doc in liver toxicity with non genotoxic liver carcinogens at the former ICI Central Toxicology Laboratory (CTL) in Cheshire UK. In 1991 he joined Rhône Poulenc and its successor companies Aventis, then Bayer CropScience. He initially worked as a regulatory toxicologist based in Research Triangle Park, North Carolina. He now leads the Research Toxicology Group at the Bayer CropScience Research Centre in Sophia-Antipolis France and is actively involved in research projects in reproductive toxicity and test methods validation in the field of endocrine disruption. His current interest is to use the "Integrative or System Toxicology" concept to find ways to interpret the early pharmacological findings detected in short term animal studies to predict adverse effects observed in the long term regulatory toxicity studies. Remi Bars is a member of the British Toxicology Society, the US Society of Toxicology and a member of the ECETOC Scientific Committee (European Centre for Ecotoxicology and Toxicology of Chemicals) where he is currently chairing the endocrine toxicity task force.

### **Dr Jenny Odum, Senior toxicologist, Regulatory Science Associates**

Jenny Odum gained her PhD at Cardiff University and has 25 years experience in toxicology in the chemical, pharmaceutical and agrochemical industries. She has a broad range of expertise within toxicological specialities and has published widely. She is an expert in the field of endocrine disruption and is a member of a number of OECD expert panels on testing for endocrine disruption. She has provided specialist advice on endocrine disruption testing and assessment and written position statements for compound defence.

Jenny has also been responsible for the scientific and technical integrity, design, conduct and interpretation of a wide range of studies involving industrial, agrochemical and pharmaceutical chemicals. These include the preparation of REACH dossiers.

### **Professor Tom Hutchinson, Programme Scientist – Environment & Health, Centre for Environment Fisheries & Aquaculture Science, UK**

Tom Hutchinson joined the UK government's Centre for Environment Fisheries & Aquaculture Science in 2009 where his work focuses on the risk assessment of natural and synthetic chemicals and nanomaterials. From 2007-2009, he was Head of Science for Environment and Health at the Plymouth Marine Laboratory, a collaborative centre of the UK's Natural Environment Research Council, where he led a research group addressing climate change, marine contaminants and risk assessment. He has over 20 years industrial R&D experience in the UK and Sweden (ICI, ZENECA and AstraZeneca; 1986-2007), encompassing both environmental toxicology and biomedical research. He was also AstraZeneca's Global Project Leader for using zebrafish as alternative models in drug discovery (2004-2006). He has a PhD in immunotoxicology from the University of Plymouth (UK) and holds honorary professorships at Brunel University (UK) and the University of Exeter (UK). Current areas of interest are the risk assessment of emerging chemical contaminants, developmental and reproductive toxicology and systems toxicology (including the use of *in vitro* and *in vivo* models to support both environmental risk assessment and also biomedical research). He is a member of the European Science Foundation and European Environment Agency working groups on the environmental risk assessment of chemicals, an active participant several OECD technical groups and also Chairs the UK's NC3Rs Ecotoxicology Working Group.

### **Dr Simon M Plummer, CXR Biosciences Ltd, Dundee UK**

Dr Simon Plummer is Head of Microarray and Bioinformatics at CXR Biosciences. Dr Plummer received his BSc (hons) in Pharmacology at the University of Dundee and PhD in Biochemical Pharmacology at the Royal Postgraduate Medical School. In addition he completed a visiting fellowship at the National Cancer Institute in Bethesda. Dr Plummer has 25 years experience in Molecular Pharmacology/Toxicology studying the mechanisms of action of carcinogens, drugs, and industrial chemicals with an emphasis in understanding effects of these agents on cell signalling pathways. Dr Plummer has extensive experience in the application of transcription profiling and bioinformatics for mechanism-based risk assessment and biomarker identification in the drug and chemical industries.

### **Dr Sue Hubbard, Principal Adviser – Product Toxicology, Rio Tinto**

Sue Hubbard has a Masters Degree in Toxicology and a PhD in Genetic Toxicology. She has worked for the UK HSE, for ICI and now with Rio Tinto for the last 17 years with current responsibility for REACH and CLP implementation. She has supported EU and worldwide industry in the GHS from almost the inception of the process and served as co-chair of the BIAC TF that advises the OECD on GHS. She was a CEFIC expert on the EU Technical Committee for Classification and Labelling Working Group (no longer in existence) and currently chairs both the CEFIC Chemical Management TF Health Working Group and the Joint ICMM/Eurometaux GHS Working Group. She has lectured widely on both general and health aspects of GHS to various organisations including assisting UNITAR with GHS training. She was an industry representative on the EU RIP 3.6 developing technical and scientific guidance (and leading the group developing the carcinogen guidelines) for GHS under CLP Regulation and the ECHA Human Health Hazard Expert Group.



