

Toxicology Group Newsletter 2022

Contents

- > Welcome from the Editor
- Committee / Keep in Touch
- Metal Ions and Antimicrobial Action a viewpoint
- Forthcoming Meetings
- Meeting Reports
- Faces of Toxicology
- Toxicology Topics in Brief
- Latest publications from WHO and IARC

Dear Readers,

Welcome to the Toxicology Group's Newsletter for 2022.

I am pleased to say that we have resumed in-person scientific meetings. Both the RSC Toxicology Award Seminar (in November 2021, that's me below, enjoying London once more) and the ever-popular Current Issues in Contaminated Land Risk Assessment (in December 2021) were run successfully as hybrid meetings. In this issue, there are meeting reports from these and other meetings that have been held.

Thanks to Jo Larner (University of Hertfordshire) for her service on the committee; she has now stood down and we recently put out a call for new committee members so I hope to introduce you to some new faces in the next issue. We are now also

holding hybrid committee meetings, which gives everyone more flexibility to participate.

Enjoy the reading, be well, and feel free to get in touch.

Kate Jones Chair, RSC Toxicology Group



Committee members

Chair: Kate Jones (HSE)

Treasurer: John MacLachlan (retired)

Secretary: Chris Waine (bibra)

Members: Lindsay Bramwell (University of Northumbria), Sarah Bull (TARA Consulting), David Hart (retired), Mark Hosford (International Platinum Group Metals Association), Anais Kahve (Exponent), Trudy Knight (Birmingham University), George Kowalczyk (Consultant), Mike Quint (Consultant), Martin Rose (Consultant), Paul Russell (Unilever), Ovnair Sepai (UKHSA), Andrew Smith (MRC-Leicester).

Keep in Touch

We now have over 750 Toxicology group members, which is great news. Some quick demographics for you:

- 36% of members are female, but 55% of under 40s are female... (let's hope we don't lose them as they progress through their careers)
 - 22% of members are under 35 and 16% are over 70
 - We have over 50 student members
- A quarter of members are based outside of the UK with USA, Hong Kong and Ireland hosting the most overseas members
 - 44% are also members of Environmental Chemistry Group

We post an eAlert every month for the group so please make sure that you are signed up to receive emails from RSC – check your account settings.

Our web pages will continue to host forms and more static content.

For more immediate updates we use LinkedIn (<u>https://www.linkedin.com/groups/12014086</u>) and Twitter (<u>@RSCToxGroup</u>). Please do join in with the conversation!





Article – Metal Ions and Antimicrobial Action

This is a personal view of one of our members, Dr Alan Lansdown FRSC (Faculty of Medicine, Imperial College, London).

Metal lons and Antimicrobial Action

Dr. Crow's paper on bioactive metal ions and their influence on superbugs makes provocative reading but the paper is sadly lacking in toxicological and clinical data (<u>Chemistry World, July 2021</u>). Whilst many transitional elements shown in the Periodic Table show evidence of antibacterial/antifungal action against selected cultured organisms and are cytotoxic in vitro, this is a far cry from the practising toxicologist or clinical scientist. Having studied the toxicology of metals for more than 40 years, I must emphasise that for many of the elements discussed in this paper, their toxicological properties far outweigh their potential clinical value in alleviating human infections.



The author enlightens us with the resurgence of interest in bismuth complexes as powerful antimicrobial agents with seemingly "very low toxicity within humans". Bismuth compounds like subcarbonate, subsilicate and subgallate were introduced into human medicine by the clinician Odier of Geneva in 1785. He demonstrated their clinical value in protecting gastrointestinal mucosae against ulcers, inflammatory disorders, diarrhoea and protozoal infections (amoeba) following oral administration. The clinical value of bismuth salts in treating the intestinal pathogen Helicobacter pylori is well documented. Insoluble basic bismuth compounds are considered to act on the bacterial cell wall and periplasmic spaces. They inhibit bacterial adherence to gastric mucosae by forming a protective coating over the mucus surfaces. Intramuscular bismuth preparations are efficacious in treating syphilis. Bismuth-containing quadruple therapy was recommended in Second Asia-Pacific Consensus Guidelines and by the Maastricht IV/Florence Consensus Report. However, like the related group 15 elements arsenic and antimony, bismuth is a toxic element, particularly following intra-parenteral injection. Principal target organs for bismuth

toxicity include brain, kidney, bone and possibly liver. Neurotoxicity is caused by insoluble inorganic bismuth compounds. Slikkerveer's group in the Netherlands have researched adverse effects of bismuth related compounds and reported mild to moderate (severe in 3% of cases) symptoms of toxicity.

The extent to which antimony compounds/complexes are used as antimicrobial agents these days is not known. I recall working with the Foundation for Sudden Infant Death Syndrome (SIDS) in the 1990's, when antimony used as a fire-retardant in cot mattresses was implicated in many unexplained child deaths. Release of stibine (SbH₃) gas or absorption of toxic antimonial substances in the presence of the mould Scopulariopsis brevicaulis were implicated but not verified. Interested readers might like to read the Warnock Report^a (1995).

Platinum-based chemotherapy (notably cis-platin) is well recognised as a potent antimitotic treatment for many types of cancer, but platinoid compounds/complexes have marginal antibacterial value in clinical practice. However, whilst cis-platin is effective against many types of human cancer, as a coordination complex, it is highly toxic and potentially carcinogenic. Recent research has identified at least 10 second-generation complexes with improved target cell efficacy and lower health risk.

My personal experience on the use and safety of silver as a broad spectrum antibacterial over many years, prompts me to draw attention to major omissions in Crow's paper. It must be emphasised that silver nitrate is probably the oldest known antibiotic with clinical reports dating back to ancient times. Katadyne technology has been used in water treatment for many years. Although silver nitrate is a highly effective broad-spectrum antibacterial against superbugs, it is corrosive and only used these days as a last resort against life-threatening pathogens like Staphylococcus aureus. Nowadays, silver-based antimicrobial preparations are used widely in modern clinics, surgical procedures and in For completeness, we should include nanoparticulate silver products, the home. prostheses, catheters, silver coatings and impregnates, and the vast range of silverrelease wound dressings, all of which have an exceptionally good safety record. Whatever the preparation, antimicrobial action is directly related to release of bioactive silver ion (Ag⁺). Few silver-resistant organisms are recorded. Fundamental research by Simon Silver's group (University of Illinois, Chicago), demonstrated the subcellular role is the Silgene complex and its relevance in regulating bacterial resistance to silver. In silversensitive bacteria, the Sil complex regulates the uptake and retention of silver ion which binds, precipitates and inactivates key enzymes with lethal effect. They have investigated the sub-cellular antimicrobial action of germanium, arsenic, cadmium, cobalt and mercury. A final point on silver should be that it is not safely (or legally) used in gastrointestinal hygiene. Much is written concerning colloidal silver, its ill-conceived use, illegal marketing and its profound risk of causing long-lasting or permanent skin and eye discolorations.

We should conclude that of the anti-superbug metals discussed, silver and probably zinc are the safest and most efficacious agents. More research is necessary on the toxicity: clinical benefit relationship for bismuth complexes.

^a https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(95)92051-X/fulltext

Forthcoming Meetings

Please take note of the following meetings and sign up early to avoid disappointment. Bursaries are available to any RSC Toxicology member for attendance at our meetings, subject to the usual conditions.

2022 Current Issues in Contaminated Land Risk Assessment

8 December 2022, London and online

An annual meeting to update those in the field on new and emerging topics in contaminated land risk assessment.

Posters are welcome - contact info@sobra.org.uk.

Toxic Tort in the UK: Current Perspectives and Recent Cases

12 May 2023, London, United Kingdom.

Following delays due to the pandemic, we are pleased to announce that planning is well underway for this event. Save the date!

A one-day event of discussion and case studies to bring together practicing lawyers and legal academics, with toxicologists and scientists, to increase understanding between the two and to understand each other's strengths and limitations.



Abstract Submissions on PEN: We welcome submissions on any relevant topic for either oral or poster presentation. The broad topics of the conference encompass • Exposure Assessment • Exposure Modelling • Toxicology • Air Pollution • Bioaerosols • Epidemiology • Aerosol Science Two internationally renowned conferences, Inhaled Particles and NanOEH are coming together to disseminate the current knowledge and understanding surrounding (nano)particle and fibre hazard, exposure and risk. This collaborative conference will be held in Manchester (UK) at the Hilton Deansgate hotel, between the 15th and 18th of May 2023.

The purpose of this joint meeting will be to bring together experts and early career researchers within the fields of occupational health and exposure, modelling, epidemiology and toxicology from academia, industry, and regulation to discuss the key aspects of the field, recent findings and how the discipline needs to move forward to answer the plethora of questions still being asked. A further key focus of this conference will be to assess the suitability and applicability of methods being utilised to answer such questions. The conference will be balanced with an integrative social schedule, as well as promoting early-career researcher development along with prizes and award lectures.

Abstracts Open Now

Meeting Reports

Plastics, From Cradle to Grave – and Resurrection III

Free online conference - 15th June 2022

Following on from the successful conferences held last year and 2019, a follow up conference was organised to expand on the key themes. As in the previous conferences we brought together academic and industrial speakers with the aim of stimulating discussion on the challenges and opportunities for researchers, industry and government. There were thematic links between micro-plastics in the environment, their toxicology and associated risk assessment; and the complex issue of the toxicological significance of the migration of recycled plastics in food contact materials.

Webinar recordings are now available.

Agenda

Micro-plastics in the Environment

- Welcome Denise Goldsmith & John MacLachlan
- Regulatory Scene Setting: Microplastics and Recycled Plastics Judy Proctor
- Exposure Source, from Bottle to Ocean Food Chain Tamara Galloway
- Characterising Microplastic Exposure and Effects Stephanie Wright
- Round Table What Do We Do About It?
 - Todd Gouin (chair), Tamara Galloway, Natalie Welden, Judy Proctor, Stephanie Wright, Caroline Gauchotte-Lindsay

Migration from Recycled Food Contact Materials

- Welcome Sally Beken & Clive Thompson
- NIAS in Food Contact Materials Regulatory Scene Setting Tim Chandler
- Characterising Exposure Chemical Analysis & Uncertainties Claire McKillen
- Characterising Toxicological Risk Jason Weeks
- Round table Should Recycled Plastics Be Used in FCM?
 - Nick Cliffe (chair), Claire McKillen, Tim Chandler, Raffi Schieir & Jason Weeks
- Wrap-up & Close Sally Beken & John MacLachlan

Toxicology Award Seminar

10 November 2021, London, United Kingdom

Professor Kelly received the 2019 RSC Toxicology Award for researching free radical/antioxidant toxicological mechanisms relevant to pulmonary toxicity, monitoring and modelling of chemicals in city air pollution and effects on human health, and leadership in the risks from compromised air quality. This seminar enabled an in-person presentation as well as an overview of Professor Kelly's research and that of several of his colleagues.

Prof Frank Kelly - Air Pollution and Health: oxidant/antioxidant wars in the respiratory tract

Dr Ian Mudway - Air Pollution Metalomics

Dr Stephanie Wright - Characterising microplastic exposure and effects

Dr Leon Barron - Rapid risk assessment approaches for emerging chemical contaminants in the environment

This was a successful hybrid event with about 25 in-person attendees and around 100 online registrants. The presentations were also recorded and made available to all Toxicology group members for a period of time after the event. Informal feedback was very good; the presentations were all excellent and, for those in the room, it was a welcome reunion with colleagues after much virtual interaction over the last couple of years.

The Toxicology Award is no longer part of the RSC's Awards offering but the committee is working on a new version – look out for a call for nominations this autumn.

SoBRA December 2021 Conference

Once again we were pleased to team up with SoBRA's annual Christmas conference, which returned in 2021 as their first ever hybrid event. The morning session featured speakers from the Environment Agency, academia and consultancies. In the afternoon session, we heard updates from the C4SL project and all the active sub-groups. This included the launch of the Asbestos Toolkit which is the final document to be produced by the asbestos sub-group. Chair Simon Cole outlined the Society's activities for this year and plans for the next.

Programme

Part 1

- Introduction Kate Jones (RSC Toxicology) and Simon Cole (SoBRA Chair)
- Recent and upcoming issues in contaminated land Theresa Cory (Environment Agency)
- Introduction to trace metal bioavailability for ecological receptors Adam Peters (WCA Environment)
- Discussion and Questions to Speakers
- Evidence review on the environmental, health and equity effects of remediation and redevelopment of contaminated sites Danielle Sinnett (UWE)
- A case study in industrial brownfield investigation, decommissioning and remediation, and the application of innovative data capture methods to support robust decision making Jess Shaw and David Atkinson (Arcadis)
- Discussion and Questions to Speakers

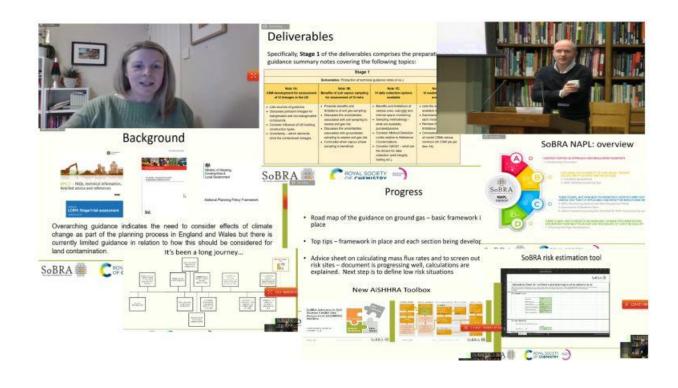
Part 2

- C4SLs Phase 2 Challenges and Outcomes Simon Firth (Firth Consultants)
- The importance of non-targeted analysis; what are we missing? David Megson (MMU)
- Discussion and Questions to Speakers
- Updates from Subgroups
 - Climate Change and Controlled Waters: Helen McMillan (RSK)
 - Vapour Intrusion: Mel Lyons (RSK)
 - Ground Gases: Steve Wilson (EPG)
 - NAPL: David Holmes (Geosyntech)
 - Asbestos including launch of the Asbestos Toolkit: Simon Coles (AECOM)
- Discussion and Questions to Speakers
- Closing Remarks Simon Cole (SoBRA Chair)

Recordings of this event that took place in December are now available to RSC Toxicology group members to view.

Part 1

https://vimeo.com/662244893/b219cea449 Part 2 https://vimeo.com/657465531/75d25d81fe



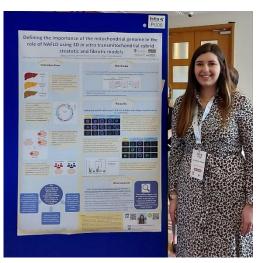


Hilton Newcastle Gateshead, 4-6 April 2022

Once again, RSC Toxicology was pleased to organise and support a special session. This year's theme was "Building confidence in computational models for decision making in Risk Assessment", chaired by Paul Russell (RSC Toxicology Group/Unilever). The speakers were:

 Qualification of the Simcyp PBK platform for confident exposure predictions - Dr Ian Sorrell (Certara, UK)

- An industry perspective strategies on using computational approaches to support decision making in next generation risk assessment - Dr Alistair Middleton (Unilever, UK)
- Computational methods for the regulatory assessment of chemicals Dr George Loizou (HSE, UK)



We are also very pleased to announce that <u>Rebecca</u> <u>Jensen</u>, PhD researcher at the University of Liverpool won the RSC Toxicology poster prize at the BTS Congress for her work on the importance of the mitochondrial genome in the role of NAFLD using 3D in vitro trans-mitochondrial cybrid steatotic and fibrotic models.

Full poster embedded below:



Faces of Toxicology



For those of you who have not yet checked out these videos, a playlist can be found <u>here</u>. This video series aims to showcase the variety of careers available in toxicology. The series begins with an animated overview of toxicology as a science followed by individual toxicologists talking about their work. The Toxicology Group Committee is working to add further videos, so if

you are interested in being a 'face' of toxicology, please get in touch.

We are continuing to add new videos; Dr Hazem Matar (dermal toxicologist, University of Hertfordshire) was added a few months back and another (Dr Fiona Sewell, NC3Rs) should be added shortly. Some of the videos are also now available on the RSC's education platform <u>A Future in Chemistry</u>.

Toxicology Topics in Brief

Some years ago, the RSC had an Environment, Health and Safety Committee (EHSC) that produced information Notes on various toxicology subjects. Several of the RSC Toxicology committee contributed to this work and the Notes were widely used in educational teaching. Following the disbanding of the EHSC, the Toxicology committee is working to refresh these old Notes (now called Toxicology Topics in Brief) and to add new topics.

The first three are now complete and available on our web page:

- Brominated Flame Retardants (BFRs)
- Endocrine Disruptors
- Food Additives

Latest publications from WHO and IARC

WHO Guidelines for Drinking-water Quality - Update to 4th Edition v

The WHO "Guidelines for drinking-water quality" provide authoritative guidance for a broad range of chemicals of potential health concern in drinking-water, along with other aspects of drinking-water quality. The latest update to the 4th edition of the WHO Guidelines has been published, incorporating the 1st and 2nd addenda.

Key updates in this latest version of the Guidelines include updated or new chemical risk assessments with accompanying management advice for asbestos, chromium, cyanotoxins, manganese, tetrachloroethene and trichloroethene.

Latest IARC Monographs Volumes 127, 128 and 129

The IARC Monographs identify environmental factors that can increase the risk of cancer.

IARC Monograph Volume 127 evaluated the carcinogenicity of some aromatic amines and related compounds, mainly chemicals used in the synthesis of dyes and pigments but also used in rubber-processing or as a reagent to separate and precipitate metals. Ortho-anisidine and ortho-anisidine hydrochloride, ortho-nitroanisole, and aniline and aniline hydrochloride were classified as "probably carcinogenic to humans" (Group 2A). Cupferron was classified as "possibly carcinogenic to humans" (Group 2B).

IARC Monograph Volume 127 - Some aromatic amines and related compounds

In IARC Monograph Volume 128, the High Production Volume chemical acrolein was concluded to be "probably carcinogenic to humans" (Group 2A), while arecoline and crotonaldehyde were concluded to be "possibly carcinogenic to humans" (Group 2B). <u>IARC Monograph Volume 128</u> - Acrolein, Crotonaldehyde, and Arecoline

IARC Monograph Volume 129 evaluated the carcinogenicity of three dyes and their precursors. Gentian violet, leucomalachite green, and CI Direct Blue 218 were concluded to be "possibly carcinogenic to humans" (Group 2B). Leucogentian violet and malachite green were "not classifiable as to their carcinogenicity to humans" (Group 3). IARC Monograph Volume 129 - Gentian Violet, Leucogentian Violet, Malachite Green,

Leucomalachite Green, and CI Direct Blue 218.

Chemistry Humour

My attempts to combine nitrous oxide with oxo cubes have made me a laughing stock.