Issue 39 Winter 2011

**Next BTS meeting:**
**BTS Annual Congress**
**25-28 March 2012**
Key Themes: Nanotechnology; Drug Discovery; Inhalation Toxicology; IVTS and ITTP Symposia; Aquatic Toxicology
University of Warwick.
**Registration Open 21st November 2011.**

## IN THIS ISSUE




The British Toxicology Society

bts
driving excellence in toxicology

# Newsletter

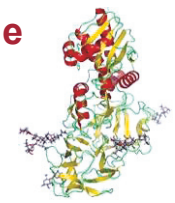
## NEWS HEADLINES

**BTS Autumn Meeting**
Nottingham Business School, Sept 2011 – see a Special Report of the Meeting inside.

**BTS to host Eurotox 2014, Edinburgh.**


**Have you tried the new BTS Website?**

**www.thebts.org**



# Editorial

My colleague Camilla Pease and I offer you a warm welcome to the Winter edition of the BTS Newsletter for 2011. We also offer our thanks to all who answered Camilla's call for contributions in the Summer Newsletter. You have given us much food for thought and we hope that many of your suggestions can be incorporated into the future Newsletters – keep them coming through the usual channels. At least one of the editors attends the Annual Congress and Autumn meeting, so feel free to make your views known in person. We also thank our regular contributors, as well as those who have written special reports. The new BTS website was launched shortly after our Summer Newsletter went to press and we hope you are using it – your feedback is welcomed.

As usual this has been an interesting issue to put together. We had a lively, well attended and exciting Autumn meeting in Nottingham, on which it was my privilege to report. The meeting included some outstanding presentations and some findings that were being reported for the first time globally, as well as one of the busiest poster sessions I have attended at a conference for some years. There is also the exciting development of our own journal, launched with the publishing division of the Royal Society of Chemistry, Toxicology Research. The editorial team joins with the Ruth Roberts and Heather Wallace in asking for all members to support this new venture – your input will be critical for its success. There are also reports from the Eurotox meeting in Paris, and Amy Mercer reports on her visit to the Gordon Research Conference, supported by the Gordon Gibson Memorial Travel Fellowship. Prof Ian Kimber, a toxicologist well known to many BTS members and a sterling supporter of industry-academia collaboration in research endeavour reflects on his contributions to immunotoxicology and to science generally, which were recently recognised by the award of an OBE, and considers the challenges facing immunotoxicology testing in the new Century. And of course our regular features are all here.

**Simon Wilkinson** (Editor-in-Chief Winter 2011 Edition)
**& Camilla Pease** (Newsletter Editor)

**Copy Deadline for the next issue:**

**1st May 2012**



**All correspondence related to the newsletter to:**

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Dr Trudy Knight
Email: t.l.knight@bham.ac.uk
Tel: 0121 414 2660

**Advertising rates:**

Full page adverts can be placed in the Newsletter at the discretion of the editor. Leaflet inserts can also be distributed with each Newsletter. Standard rates are as follows :

Books, journals and services: £250
Positions vacant: £750
Reductions are negotiable for multiple adverts and for non-profit-making organisations.

Please contact the treasurer Guy Healing for further details.
Email: Guy.Healing@astrazeneca.com

**All enquiries regarding BTS matters, including membership to:**

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Tel: +44 (0) 1206 226 059 Fax: +44 (0)1206 226 057
Email:secretariat@thebts.org
BTS website: www.thebts.org

# Society News & Notices

## President's Address

Sitting on the train on the way back from our annual Officers' meeting, I am reflecting on what the officers and the society has achieved over the last 12 months. At this time last year we devised a 5-pillared, 5 year strategy that was presented at the AGM Spring 2011. Each of the strategic aims had specific detailed delivery tactics; we reviewed these today and I think we were all pleasantly surprised by how much of what we intended has come to pass!

Key to highlight under 'sustainability' was the need to secure and stabilize finances for the future – we reviewed this today and thanks to our treasurer Guy Healing and the FSC, we are in a much stronger position in terms of balancing income and expenditure. Another key driver under 'promote the science of toxicology' was the development and launch of the new website which happened recently thanks mainly to Paul Duffy and the CSC, Linda Allardyce at PCS and Heather Wallace, our GS. Along with this, we have a new pro-forma for proposing sessions for the scientific meetings so please share your ideas with us. Also notable under 'drive the science' was the aim to maintain and enhance the quality of our scientific meetings. I am sure that you will agree that these have been a big success under the guidance of Ted Lock, Shirley Price and the SSC. Under 'the toxicology society of choice' we also took an action to seek opinions on different ways to run our annual congresses; based on feedback we have taken a decision to try a hotel venue for the first time in 2013 (St John's Hotel, Solihull, 7th-10th April 2013). We look forward to your feedback on your experience of this different approach.

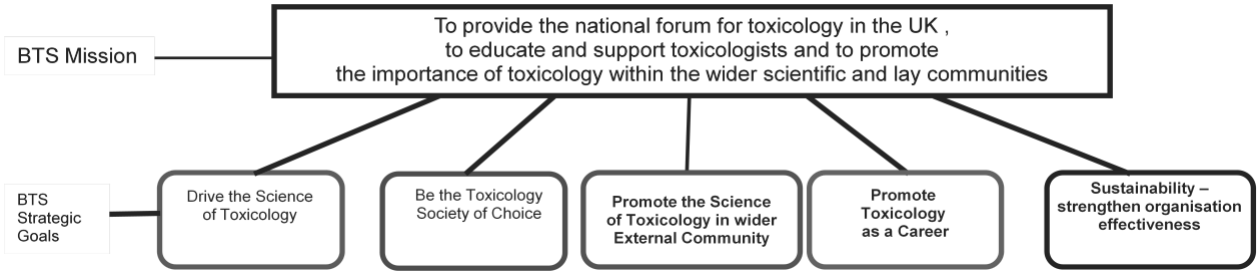
On a different note, we were all very proud to see the BTS nomination for the EUROTOX Bo Holmstedt award go to our own Professor Gerry Cohen. Gerry gave an outstanding lecture at EUROTOX in Paris entitled 'Apoptosis: a stressful journey from barnacles to cancer'. Many agreed that this was the best presentation of the meeting: BTS attendees will have the chance to hear Gerry's lecture since he will deliver the BTS Barnes Award Lecture in 2012 at our annual meeting in Warwick.

As I mentioned earlier, we have taken steps to stabilize our finances and to balance income and expenditure. However, we have taken a clear decision to continue sponsoring our meetings upfront, donating £7500 and £21000 to the Autumn and Main meetings, respectively. We continue to believe this is a good use of society assets since we know that you, the membership, value these meetings above all other things offered by our society.

As ever, we depend on you for your support so please offer any thoughts on the steps we have taken and any ideas new you may have to me or any of the Officers of the society.

### Ruth Roberts (Astra Zeneca)

*The Newsletter Editorial team are delighted to congratulate Ruth on her recent election to Fellowship of the Royal College of Pathologists.*



# Society Officers & Committees 2011-2012

## Executive Committee

| | |
|---|---|
| President | Prof R Roberts |
| Vice-President | Prof I Kimber |
| General Secretary | Dr H M Wallace |
| Treasurer | Dr G Healing |
| Scientific Meetings Secretary | Prof S Price |
| SSC Chair | Prof E Lock |
| Ordinary Members | Drs M Wright, C Powell, J Haselden, R Jefferson<br>Prof N Gooderham,<br>Mr A Woolley |
| Co-opted Members | Prof K Chipman (past president)<br>Dr J Kilgour (ESC),<br>Dr P Duffy (CSC)<br>Dr D Mason (ECTSC) |

## Fellowship Committee

| | |
|---|---|
| Chair | Prof R Roberts (president)<br>Prof Ian Kimber (president elect)<br>Prof K Chipman (NSC)<br>Prof E Lock (SSC),<br>Dr H M Wallace (General Secretary) |

## Scientific Sub-committee (SSC)

| | |
|---|---|
| Chair | Prof E Lock |
| Scientific Meetings Secretary | Prof S Price |
| Abstracts Editor | Dr D Williams |
| Special Editions Editor | Prof G Hawksworth |
| Ordinary Members | Drs T Gant, J Tugwood, M MacFarlane,<br>M Beaumont |
| Co-opted Members | Dr G Healing (Treasurer)<br>Dr D Mason (ECTSC)<br>Dr J Kilgour (ESC)<br>Dr P Duffy (CSC),<br>Dr R Gibson (IVTS)<br>Dr A Smith (ITTP)<br>Dr J Barnes (BSTP) |

## Education Sub-committee (ESC)

| | |
|---|---|
| Chair | Dr J Kilgour |
| Secretary | Dr N Plant |
| Ordinary Members | Drs J Burnett, M Chapman<br>R Chilcott, S Chivers<br>S Creton, N Hodges |
| Co-opted Member | Dr D Gray (ECTSC) |

## Nominations Sub-committee

| | |
|---|---|
| Chair | Prof K Chipman<br>Profs G Hawksworth & A Vale (past presidents)<br>Prof E Lock (SSC) |
| Ordinary Members | Prof P Goldfarb<br>Prof A Boobis<br>Dr A Woolley,<br>One vacancy |

## Finance Sub-committee

| | |
|---|---|
| Chair | Prof I Kimber |
| General Secretary | Dr H M Wallace |
| Treasurer | Dr G Healing |
| Ordinary Members | Prof E Lock (SSC), |
| Co-opted Member | Prof S Price<br>One vacancy |

## Communications Sub-committee (CSC)

| | |
|---|---|
| Chair | Dr P Duffy |
| Secretary | Dr T Knight |
| Ordinary Members | Drs P Harrison,<br>J Howarth,<br>S Moore,<br>D Shaw,<br>C Pease & S Wilkinson (Newsletter editors) |
| Co-opted Members | J Kilgour (ESC),<br>T Cull (ECTSC) |

## Early Career Toxicologists Sub-committee (ECTSC)

| | |
|---|---|
| Chair: | Dr D Mason |
| Secretary: | Dr M Cush |
| Ordinary Members | Dr D Antoine, I Copple,<br>T Cull, S Iqbal,<br>Dr A Mercer<br>T Mullaney, D Gray,<br>Dr L Randall |

## CPD Group

| | |
|---|---|
| Chair | Dr H Wallace |
| Ordinary Members | Drs J Foster, P Duffy<br>C Springall, S Sparrow<br>S Price, S Crome |

## Speciality Section Chairmen

| | |
|---|---|
| Speciality Section Liaison Officer | Dr M Wright |
| Discovery Toxicology | Dr J Hitchcock |
| Human Toxicology | Dr J Thompson |
| Immunotoxicology/Allergy | Prof I Kimber |
| Biotechnology | Vacant |
| Nanotoxicology | Dr S Hankin |
| Occupational Toxicology | Dr A Mallett |
| Regulatory Toxicology | Mr H Stemplewski |
| Risk Assessment | Dr C Courage |

## Affiliated Society Link

| | |
|---|---|
| In Vitro Toxicology Society | Dr R Gibson |
| British Society of Toxicological Pathologists | Dr J Barnes |

## Other Positions

| | |
|---|---|
| Newsletter Editors | Dr C Pease<br>Dr S Wilkinson |
| Newsletter Editorial team | Dr P Baldrick<br>Dr G Healing<br>Dr T Knight |

Changes to committee membership should be notified to Heather Wallace, General Secretary.

h.m.wallace@abdn.ac.uk

For further information see www.thebts.org or contact:

BTS Administration: secretariat@thebts.org

# Awards & Opportunities

## Fellowship of the British Toxicology Society (FBTS)

The AGM in 2005 supported the establishment of the Fellowship of the British Toxicology Society. The names of the first group of Fellows were given in the Summer 2006 issue of the newsletter. In addition, those holding Honorary Membership Status automatically became Honorary Fellows. Further announcements of the names of Honorary Fellows and BTS Fellows were announced in the Summer 2008 and Summer 2009 issues of the newsletter.

**Criteria for the award of the Fellowship of the British Toxicology Society**

- The individuals nominated will have made substantial contributions to the discipline of toxicology.
- Nominees will usually have been members of the British Toxicology Society for at least seven years.
- Members of the British Toxicology Society who are nominated as Fellows will not only have made a substantial contribution to the discipline of toxicology, but will also normally have made a considerable contribution to the work of the Society.
- Those who exceptionally are not members of the Society will have made distinguished contributions to toxicology at the National and International level but have a primary affiliation to another discipline.
- In future the Honorary Fellowship will replace Honorary Membership.

### Appointment of Fellows

- The Executive Committee will be responsible for agreeing the nominations on the advice of the Fellowship Committee, composed of the President, Past President (Chairman of the BTS Nominating Committee), President-Elect and Chairman of the Scientific Sub-Committee.

**Subscription for Fellows**

- Fellows of the British Toxicology Society will pay the same rate as ordinary members.

**Honorary Fellows will not pay a subscription.**

### The Paton Prize

The Society was left a generous bequest by Sir William Paton to encourage scholarship in the historical aspects of toxicology. Sir William Paton's donation was matched by the British Toxicology Society to establish the Paton Prize. The prize is offered biannually. The Society has interpreted Sir William's wishes broadly. Recipients will be asked to present a lecture at the Annual Congress followed by a publication in an appropriate journal.

**Recipients of the award:**

| | |
|---|---|
| 1998 | Prof R Smith |
| 2000 | Prof P N Magee |
| 2002 | Prof R Estabrook |
| 2004 | Dr I Purchase |
| 2006 | Prof J Ashby |
| 2008 | Prof G G Gibson & Prof P S Goldfarb |
| 2010 | Dr F M Sullivan |

### The John Barnes Prize Lectureship

This prize lectureship was established in memory of Dr John Barnes, a pioneer in scientific toxicology. The John Barnes lecture is presented at the Annual Congress. The first award was made in 1979 to Professor W. N. Aldridge. The membership is asked to propose suitable recipients and the lecturer is selected following recommendations from the Scientific Sub-Committee and Executive.

**Recipients of the award:**

| | |
|---|---|
| 1979 | Prof W N Aldridge |
| 1981 | Prof P N Magee |
| 1983 | Prof L Golberg |
| 1985 | Dr J Cairns |
| 1987 | Prof G Zbinden |
| 1989 | Prof B N Ames |
| 1991 | Prof S Orrenius |
| 1993 | Prof J A Swenberg |
| | Dr F De Matteis |
| 1995 | Prof R Lauwerys |
| 1997 | Dr M K Johnson |
| 1999 | Prof A Wyllie |
| 2001 | Sir Alex Jeffries |
| 2003 | Prof J Peto |
| 2005 | Prof J Goodman |
| 2007 | Prof D S Davies |
| 2009 | Prof R Schulte-Hermann |
| 2011 | Prof R Wolf |

### Early Career Investigator Award

Details of this award and how to nominate a potential recipient are given within this issue.

**Recipients of the award:**

| | |
|---|---|
| 2001 | Dr Elizabeth Martin |
| 2002 | Dr Camilla Smith Pease |
| 2003 | Dr Dean Naisbit |
| 2004 | Dr Nick Plant |
| 2005 | Dr Jonathan Moggs |
| 2006 | Dr Dominic Williams |
| 2008 | Dr Daniel Smart |
| 2009 | Dr Jean-Lou Dorne |
| 2010 | Dr Muireann Coen |
| 2011 | Dr Karen Swales |

### Student Prize

This prize is awarded for the best presentation of a poster or oral presentation by a student at a BTS Meeting. It is judged by a panel of judges appointed by the Meeting Scientific Organiser and the prize is normally presented at the Conference Dinner.

## British Toxicology Society Bursaries

**Criteria for eligibility**

The British Toxicology Society awards bursaries for students or junior scientists in non-profit making educational or research organisations to support their attendance at EUROTOX and IUTOX meetings in addition to bursaries for domestic BTS meetings. The criteria for eligibility are:

**BTS Meetings**

- bursary applicants must be members of the BTS at the time of application
- Applicants can receive a maximum of 3 bursaries
- Presentation of a poster or oral communication
- Research student or junior scientist employed by a non-profit making educational or research organisation. Status must be confirmed by head of department.
- Submission of a written report on the meeting for inclusion in the BTS Newsletter. More info or submission of report to editor@thebts.org

**EUROTOX and IUTOX Meetings**

- As above, plus the following conditions:
  - Membership of BTS for at least 1 year
  - No previous equivalent bursary will have been received
  - Applicants may receive either a EUROTOX or IUTOX bursary

**Making an application**

**BTS Meetings**

Deadline for bursary applications for the Annual Congress 2012 meeting is **21 January 2012**
To be sent to:

Professor Shirley Price, University of Surrey
Email: s.price@surrey.ac.uk

**EUROTOX and IUTOX Meetings**

Applications for EUROTOX and IUTOX bursaries must include a:

1. Short curriculum vitae
2. Supporting letter from Head of Department
3. Clear statement of other support sought or obtained
4. Copy of the abstract

These may be sent at any time to:

Professor Shirley Price, University of Surrey
Email: s.price@surrey.ac.uk

Applications will be reviewed at the first opportunity by the Scientific Sub-Committee, taking into consideration a number of factors, including the quality of the abstract.

The Scientific Sub-Committee normally meets four times per annum so candidates for EUROTOX and IUTOX bursaries are advised to submit their application at least three months in advance of the registration deadline. Applications should be submitted along with the abstract.

## Early Career Investigator Award

An 'Early Career Investigator Award' is presented annually by the British Toxicology Society. The award is made in recognition of their contribution to toxicological sciences. This contribution may take the form of a single seminal piece of work or sustained achievement in an area of toxicology.

The award will be presented at the British Toxicology Society Annual Congress normally by the Chairman of the Scientific Sub-Committee.

The award will comprise a plaque and a cheque for £500. The successful candidate will be invited, at the Society's expense, to the Congress and will be expected to make a presentation which will be published in the journal Toxicology.

Candidates should have no more than 10 years postdoctoral or 14 years postgraduate experience on the 1st January preceding the BTS Annual Congress, and must be a current member of the Society. Nominations should include a:

(1) full *curriculum vitae* (including a list of all publications),

(2) copy of four publications by the candidate (industry based candidates may submit alternative documents that confirm their scientific contributions),

(3) 1000 word description of the candidate's achievements and

(4) letter of recommendation from the member's supervisor or other senior toxicologist.

Nominations for the 2011 award should be forwarded to the Chairman of the BTS Scientific Sub-Committee, Professor E A Lock, School of Pharmacy & Biomolecular Sciences, Liverpool John Moores University, Byrom Street, Liverpool, L3 3AF by the end of December 2011.

# Norman Aldridge Travelling Fellowship

Each year the British Toxicology Society invites applications for the Norman Aldridge Travelling Fellowship. This Fellowship, in memory of Dr Aldridge's contribution to toxicology, is to enable a young EU based scientist to advance and broaden his/her research in toxicology. The applicant (typically postdoctoral or nearing the completion of a Ph.D) will visit 1 or 2 key laboratories, in a country outside the UK (for UK based applicants) or in the UK (for European based applicants). The successful applicant will be a member of a European Toxicology Society.

The value of the Fellowship will be up to £1000. Applicants must first make preliminary arrangements with the laboratory(ies) they wish to visit. The application should include:

- A curriculum vitae.

- Details of the purpose of the proposed visit.

- arrangements the applicant has made with the receiving laboratory

- financial arrangements relating to the visit, including information on any other awards that will contribute to the costs.

A letter of recommendation from the Head of Department where the applicant is working and from the laboratory the applicant proposes to visit.

Applications will generally be reviewed by the Scientific Sub-Committee of the British Toxicology Society and should be sent by 15th January 2012, to Professor E A Lock, School of Pharmacy & Biomolecular Sciences, Liverpool John Moores University, Byrom Street, Liverpool, L3 3AF.

The successful applicant will be expected to submit a short report highlighting the outcomes of their visit which will be published in the British Toxicology Society newsletter.

The Committee reserves the right to recommend changes to any aspect of a proposal or not to make an award in a year when no suitable applications have been received. Successful applicants will not be eligible for the award on a subsequent occasion.

## BTS ANNUAL CONGRESS 2012
## 25 – 28 MARCH 2012,
## UNIVERSITY OF WARWICK

**Registration and Abstract Submission Now Open!**

**Key Dates:**

Registration Open: 21st November 2011
Abstracts Open: 21st November 2011
Abstracts Close: 20th January 2012
Early Bird Registration Closes: 20th February 2012

**Key Themes:**

**Plenary Lecture – "The new toxicology of sophisticated materials: Nanotoxicology & Beyond"**

**Professor Martin Philbert, University of Michigan, USA**

Nanotechnology
Drug Discovery
"What's so different about inhalation anyway?"
organised by the Association of Inhalation Toxicologists
IVTS Symposium
ITTP Symposium
Aquatic and Environmental Toxicology
Continuing Education Programme - "New Approaches to Environmental Toxicology",

**** New for this Congress*****
Hot Topics Lecture in the area of Genetic Toxicology

**Full details on the BTS website www.thebts.org**

# Report from the BTS Autumn Meeting – Nottingham Business School, 5-6 September 2011


## Reports from the Main Sessions

### Symposium 1 Safety Assessment of Novel Therapeutic Agents

***BTS President Prof Ruth Roberts, during her welcoming address***

The Annual Congress began with a warm welcome from the BTS President, Prof. Ruth Roberts (AstraZeneca, UK) who handed over to Dr **Tim Gant** (Leicester University) and Prof **Shirley Price** (University of Surrey) co-chairs for the first symposium, which covered the requirements for safety assessment for novel therapeutics such as oligonucleotides and antibodies. The first talk was given by **Dr. Kevin Brady** (Bicycle Therapeutics Ltd, Cambridge, UK), who gave an excellent presentation on in vitro ADME assessments for oligonucleotide-based therapeutics. Dr Brady gave a clear overview of the current therapeutic agents available or in development and their modes of action (siRNA, antisense RNA and antisense Gapmers), before continuing to explore the pre-clinical development of these molecules. One of the key challenges was delivery; how to direct highly charged relatively large molecules which cannot penetrate lipid membranes towards their targets inside the cell, whilst avoiding lysosomal delivery and destruction by endonucleases. The mode of delivery often impacted directly or indirectly on toxicity, though there was often little relevance between in vitro delivery systems (such as lipid transfection) and strategies employed in vivo. The key toxicology aspects covered included innate immune system activation, promiscuous binding to other RNA species and "swamping" endogenous pathways with the expressed agent. It was critical to assess immune activation by evaluating cytokine pathway stimulation, as this can confound potency as well as producing undesirable toxic effects; certain modifications e.g. 5-methyl cytosine can reduce the risk of immune system activation. Oligonucleotides require careful design to avoid promiscuous binding, and good methods for identifying this effect were now available for the "parent" therapeutic, though metabolites and impurities were more difficult to assess. Dr Brady also underlined the importance of competition (especially for siRNA) with microRNA for the RNA-induced silencing complex RISC, and described some of the strategies employed to avoid abolition of microRNA export from the nucleus.

The next talk was given by Dr **Steve Hood** (GSK Research and Development, Ware, UK), who gave an account of the pitfalls to progress for novel oligo-based medicines from the bench to the clinic. Although the potency of such agents could be "designed in", the high cost of materials and class-related off target toxicities meant that therapeutic index, cost benefit and market position had to be balanced with potency. Dr Hood described the journey for one such therapeutic in development as a potential treatment for Duchenne Muscular Dystrophy, the exon-skipping antisense oligonucleotide GSK2402968. This oligonucleotiide overcomes deletions in the dystrophin gene to yield a shortened version of the wild type protein which retained functionality. The first hurdle to be cleared was delivery to the target (the muscle). This process was aided by the fact that diseased muscle was "leaky" and took up more oligonucleotide (which is delivered "naked" than healthy muscle. The target for subcellular delivery for this agent is cell surface receptors, but the majority of targets are not on the cell surface, resulting in endosomal uptake; late endosomes are effectively "acid baths". Area under the curve of GSK2402968 for liver and kidneys was some fifty-fold greater than for plasma; liver and kidneys were also the sites of proinflammatory histopathological changes and chronic toxicity. There were a number of other "quirky" toxicity findings, such as coagulation prolongation and complement activation in monkeys. Clearance from plasma was rapid but much slower from liver and muscle (the agent was still detected in muscle 100 days after

dosing), questioning the relevance of plasma pharmacokinetics. A major challenge for oligonucleotide therapeutics was that they were treated as “big small” molecules, making their safety assessment expensive. During questions, Dr Hood noted that since impurities may have the potential for pharmacological effect, much hard work was put into control of the impurity profile. The longer half life in the kidney than plasma was due to formation of basophilic granules in the renal tubular cells of the cortex.

This was followed by an account of a survey of animal use in in vivo safety assessment of monoclonal antibody (mAbs) based therapeutics by Dr **Kathryn Chapman** (NC3Rs, UK). The study was part of an ongoing, six year project involving the NC3Rs and a number of industrial partners in which safety assessment data were shared before regulatory approval, in order to yield useful information, shape regulatory change and future research development. Some 30 mAbs were now approved for therapeutic use, with another 300 in the development pipeline. Increasing manipulation of mAbs was now possible and the number of potential targets was increasing. There had recently been an increase in the use of primates in safety studies for mAbs, although some mAbs were human specific so other surrogates such as transgenic mice were needed to identify good biomarkers for work in the clinical phase. The project had identified that, although many mAbs had no relevant potency in species other than non-human primates, a significant number (16 out of 86) also showed potency in rodents. Forthcoming legislation (from ICHS6 (R1)) paved the way for increased rodent use, giving the opportunity for the main safety study to be carried out in rodents, if there were no immunogenicity or ant-drug antibody issues. There were also opportunities to reduce the use of non-human primates in safety studies to make the studies more efficient, by reducing the number of dose groups, the number of recovery animals and the number of animals in the main dose groups, without detriment to safety assessment. Toxicity that was unrelated to pharmacology was only very rarely observed. There were considerable upwards pressures on the expected use of non-human primates, as the size of the mAb portfolio increased, along with the requirement for large and expensive developmental and reproductive and juvenile toxicology studies. Dr Chapman recommended that rodent species should be considered for chronic toxicology studies, and the main study should be a three plus three group size, with two plus two for recovery animals, the latter in control and high dose groups only (though it was pointed out that it was feasible to do recovery with intermediate dose rather than controls). Short term study findings should be used to inform longer term studies. Regulatory guidance on the re-use of primates in safety studies for mAbs was expected to emerge (it was already used for other biotechnology entities).

***Presenters at Symposium 1 (left to right) Dr Lee Coney, Dr Kathryn Chapman, Dr Kevin Brady, Dr Steve Hood and Dr Jane Stewart***

Dr **Jane Stewart** (AstraZeneca, UK) outlined the developmental and reproductive toxicity testing requirements for bioproducts. A recurring theme throughout the symposium was that species selection (i.e. one which demonstrates the anticipated pharmacodynamic response) was key and DART testing was no exception. The requirements for testing small molecules were fertility (rodent only); embryofoetal development (first trimester) in rodents and rabbit; and pre-/post-natal development in mother:offspring pairs (rodent only). ICHS5 required testing in at least one pharmacologically relevant species, and since off-target toxicities were rare, one species was usually acceptable, especially if that species was a non-human primate. Although animals were dosed on the basis of the expected pharmacological effect, our understanding of such effects remained limited, so it was important that unintended consequences were recognised. The cornerstone of male fertility testing in non-human primates was weight and histopathology of the testes; mating studies were not feasible and longitudinal semen analysis was required only if the target was in the male reproductive tract. However, hazard detection was difficult, as imperfect testicles may be a consequence of life in cynomologous colony. Functional fertility testing in females was not possible so surrogate endpoints were used, such as the normal menstrual cycle using daily vaginal swabs, although these were difficult to interpret, as male and female animals may not be brought together until immediately prior to the test. However, the menstrual cycle is a good indicator of suitability for testing. Our knowledge of histiotrophic support in early gestation is very poor compared to our understanding of the chorionallantoic placenta. The anatomy of the chorionallantoic placenta differed significantly between animals, especially in the number of surrounding tissue layers, hence the choice of species would markedly influence transfer of large molecules to the embryo. An enhanced pre

and post natal development study design using cynomologous monkeys is often employed, in which a single cohort of pregnant animals is dosed throughout gestation and the functional and morphological consequences in the infants are monitored, for as long as the organ of interest determines e.g. up to six months old for immune function. Case studies showed that adverse effects were almost always predictable from the primary pharmacological effect and hence considered directly relevant to man (and to subsequent labelling). The results of studies were now appearing in the open literature with the result that the strengths and weaknesses of various study designs were revealed, which was considered a step forward. One limitation of the use of non-human primates was the small number of offspring (usually about twelve in cynomologous monkeys) which made detection more difficult.

The final talk in the first symposium was by Dr. **Lee Coney** (Huntingdon Life Sciences) who gave an excellent account of safety assessment of novel "biologics", a convenient catch-all term used to describe a diverse range of entities. Dr Coney highlighted that all such safety assessment is approached on a case-by-case basis, even within the same product class. An understanding of the biological mechanisms involved was critical, as was the requirement to reproduce this in toxicology testing species. Relevance of the animal model to potency in humans must be demonstrated, as must the appropriate pharmacodynamic response. Key considerations were the intrinsic toxicity of the delivery system, the vector or virus employed, transgene (over) expression, interaction of the gene product with endogenous pathways and activation of the host immune system. Other factors that required consideration were DNA tissue distribution, insertion into the host genome, formulation toxicity, autoimmunity, viral vector considerations (shedding in non-target tissues, immune response, inflammatory response, insertional mutagenesis, and recombination during manufacturing) as well as the immunomodulatory effects of adjuvants. On and off-target effects were often difficult to distinguish because of interference with cascades; our understanding of the biology was still developing. The optimal solution was toxicology studies with the therapeutic candidate in one pharmacologically relevant species, given that ethical considerations always apply. Where no such studies are possible, it was possible to use models using surrogate (homologous) genes (given sufficient knowledge of how expression of surrogate genes differed from the intended candidate), transgenic animals expressing the human gene, or disease models. The clinical route of administration should be used in tox studies, and all intended doses should be assessed for margin of safety (not always easy because of potency). The duration of the study should cover the length of expression (or longer in recoverability studies). Biodistribution was critical, as was integration (which was required by regulators for non-life threatening diseases; integration into the germ line was absolutely prohibited). Immunogenicity was important if it affected the PK/PD profile of the transgene, but was not necessarily a problem otherwise.

***Report by Simon Wilkinson***

## Short oral presentations

**Chair: Professor Ted Lock (Liverpool John Moores University, UK).**

The first short oral communication was given by **Ishani Kar-Purkayastha** (UK Health Protection Agency), who described an investigation into ill health in workers (and their families) resulting from lead exposure during stripping of lead casings from copper telephone cables at a metal recycling plant. The chronic effects of lead are particularly significant for cognitive development, with some researchers suggesting that neurocognitive effects can occur at blood lead levels as low as 10 µg/dl. Following an HSE inspection at the plant, control measures were advised and occupational health input was sought. Of 92 workers assessed, 90 had elevated blood lead levels, six workers were symptomatic and three required chelation therapy. A subsequent public health investigation revealed the potential for other outside the workplace to be exposed, and household contacts were screened. The workers were all immigrant workers who lived in large households with considerable contacts and movement between the country of origin and the UK. Three children with blood levels of concern were identified, though no symptomatic individuals were found. Investigation of the household environment identified no other source. There were a number of factors that contributed to the exposure: non compliance with health and safety procedures, language barriers and low levels of literacy and clustering of multiple vulnerabilities (type of employment, large household, mobile population, non-registration with local primary healthcare).

**Dr Kate Jones** from the Health and Safety Laboratory (UK) reported on human volunteer studies to determine toxicokinetic interactions between three pesticides, deltamethrin, pirimicarb and chlorpyrifos methyl following oral administration at the acceptable daily intake. In vitro studies with these agents had identified only additive effects; deltamethrin hydrolysis was inhibited by chlorpyrifos, chlorpyrifos oxon and malaoxon, but not by malathion. The human volunteer studies did not detect any interactions between deltamethrin and chlorpyrifos methyl or between pirimicarb and chlorpyrifos methyl. The mean half life of all three agents showed no difference between single and combined dose.

**Muhammad Farooq** (University of Aberdeen, UK) gave a talk on the role of pregnane X receptor (PXR) and farnesoid X receptor (FXR) in the regulation of rat hepatic uptake transporters. Nuclear receptors such as PXR and FXR were well known to regulate phases I to III of xenobiotic metabolism. PXR for example was involved in regulation of liver cholesterol transformation into bile acids and bile acid hydroxylation, sulphation and glucuronidation and export via MRP3 and MDR1. FXR is involved in chlostasis; disruption of FXR is the predominant effect in cholestasis-related disorders such as progressive familial intrahepatic cholestasis (PFIC). PFIC type 1 is associated with down regulation of FXR (PFIC 1 patients lack the BSEP transporter, a primary target of FXR). The aim of Muhammad's study was to carry out absolute quantification of FXR and PXR in vitro, quantitate uptake transporters OAPT1A4 and NCTP at the mRNA level and evaluate the co-ordinated role of PXR and FXR, using hepatocytes cultured using the sandwich system. PXR ligands (dexamethasone, spironolactone and pregnenolone 16α-carbonitrile) increased expressed of PXR but did not influence FXR expression, whilst FXR ligands (chenodeoxycholic acid, GW4064 and 6-ethyl chenodeoxycholic acid) increased expression of both receptors. PXR ligands induced expression of Oatp1a4 and Nctp, whilst FXR ligands down regulated both transporters. FXR effects dominated when ligands were co-adminstered. Potent agonists for PXR/FXR were potential candidates for treatment of cholestasis. Muhammad noted that the rat appeared to be a better model for human PXR and FXR regulation than the mouse.

***Symposium report by Simon Wilkinson***


***Oral communications presenters (left to right) Ishani Kar-Pukayastha, Kate Jones and Muhammed Farooq, with Scientific sub-committee chair Ted Lock.***

## Poster Communications

The poster session was one of the liveliest and best attended sessions I have attended at any conference, and interest in the posters was indeed so intense (even in my own poster) that I didn't get the chance to take any pictures. All the posters I got the chance to look at were of a very high standard of scientific rigour and presentational quality. Amongst those which caught my interest were two posters by Odu Okoturo-Evans and co-workers from Imperial College, London, the first of which was on the effects of multi-walled carbon nanotubes on proteomics of A549 lung epithelial cells. A dose related reduction in expression of a number of important proteins was found at concentrations which did not influence viability, especially ribosomal proteins, suggesting effects on protein synthesis pathways. The second poster from this group described the responses of protein expression profiles (using SELDI-TOF-MS) in cultured human neuronal cell lines to a range of pyrethroid pesticides, in order to identify common mechanism groups to streamline the risk assessment process. Protein expression profiles were able to classify the different pyrethroids into two groups, dependent on their differential influence on the three different cell lines employed. Further analysis on a representative group of compounds showed changes in protein expression that were specific to each compound. Vicki Stone and co-workers from Herriot-Watt University described progress on a pan-European project comparing the toxic effects of a panel of ten nanomaterials in a diverse range of in vitro models. These tests have grouped the nanomaterials into two groups on the basis of their effects on pro-inflammatory cytokine production at sublethal concentrations and show good agreement with in vivo models, though there was a strong modulatory effect of the different dispersants used. Lung-lining fluid resulted in a marked increase in cytokine production with Au nanoparticle treatment in macrophages and hepatocytes compared to serum. Andrew Axon was awarded the BTS Poster Prize for his poster on tartrazine as a human estrogen receptor ER-β agonist, hepatotoxin and role in the causation of cholestatic liver injury. Andrew's research demonstrated that chronic exposure resulted in significantly increased portal tract inflammation and collagen deposition, as well as down regulating expression of the bile salt transporter MRP3 in mice. Posters by Muhammad Farooq on PXR/FXR involvement in the regulation of hepatic efflux transporters and Giovanni Pellegrini on histopathological and ultrastructural changes in pulmonary epithelial cells in response to oral thiourea in Wistar rats were highly commended.


***Andrew Axon (Newcastle University), with his winning poster***

***Presenters commended for their posters, with members of the judging committee (left to right): Prof Gay Hawksworth, Dr Dominic Williams (judges), Muhammad Farooq, Giovanni Pellegrini and Dr Marion McFarlane (judge)***

***Report by Simon Wilkinson***

## Continuing Education Programme: Toxicology and Risk Assessment of Chemical Mixtures

**Chair: Professor Shirley Price (University of Surrey, UK)**

There was only one presentation in the CEP course. **Professor Len Levy** (Institute for Environmental Health, Cranfield, UK) gave an excellent summary of potential strategies for dealing with chemical mixtures in risk assessment. Although current risk assessment approaches are largely based on evaluating the toxicology of a single compound (a route which the REACH registration process reinforces), the reality was that individuals were exposed simultaneously to a mixture of compounds, and indeed even chemicals with a single compound name on the label could, according to EINECS classification rules, contain up to 20% by weight of impurities. Prof Levy outlined the approach described by the Interdepartmental Group on the Health Risks of Chemicals in their guidance document "Chemical Mixtures: a framework for assessing risks to human health" which was available free as a download from the IGHRC website. Prof Levy described the different types of mixture (simple and complex, manufactured, process emissions etc) and how mixtures might act differently from single compounds (chemical-chemical interaction, toxicokinetic and toxicodynamic interactions). The guidance from IGHRC was a multi step decision tree which involved definition of the mixture, identification of exposed populations, characterisation of hazards, gathering evidence for interactions, selection of an appropriate interaction model, characterisation of mode of action of each component, and identification of a cause for concern. Prof Levy made it clear that the guidance was just that, with no regulatory power, and that very often there were insufficient data available to perform a risk assessment for some mixtures, and in such cases, exposure limits could be amended to reflect this.

***Report by Simon Wilkinson***

## Symposium 2 Pesticides: Lessons from the Last Decade

**Chairs: Professor Gay Hawksworth (University of Aberdeen, UK and Professor Ted Lock (Liverpool John Moores University, UK).**

A comprehensive overview of the concerns regarding previous and future use of organochlorine pesticides such as DTT was given by **Dr Andrew Smith** (University of Leicester, UK) in his talk; DDT past and present. Andy discussed the transition of DTT from a miracle compound upon its discovery in the middle part of the 20th century, to the perceived toxicological nightmare it presents today. The history of the early manufacture and uses of DTT and its remarkable versatility, and the modern understanding of its persistence, accumulation and toxicity were described in an entertaining presentation. DDT has been shown to be less acutely toxic than some other pesticides such as lindane and dieldrin, though the potent androgen disrupting activity of p,p'DDE was demonstrated in 1995, resulting in a ban for many types of usage in 2001. However, DDT remains licensed for indoor spraying. Convincing evidence for human health risks from this latter activity remains sparse, and must be balanced against malaria risk.

**Dr Phillip Botham** (Syngenta, UK) gave a talk entitled Paraquat and Parkinsons – The state of play. This talk covered the evidence supporting the links between exposure to certain pesticides and an increased risk of developing Parkinson's disease (PD). Paraquat (PQ) exposure has been highlighted as a risk factor for PD because of its structural similarity to MPTP and its active metabolite, MPP+, a chemical that is known to damage dopaminergic neurones via oxidative stress. Recent data in mice have shown that the common belief that PQ cannot cross the blood-brain barrier is incorrect, and in vivo models show that PQ can accumulate in the brain,

though concentrations were much smaller than in other organs, and there was no accumulation in the substantia nigra. Penetration of porcine blood brain barrier by PQ was very poor. The reality of the current understanding, or lack thereof, between PQ exposure and PD was described, and there was an enlightening discussion of conflicting and inconsistent findings both from epidemiological studies and in vivo models. This was especially the case with literature reports of the loss of tyrosine hydroxylase positive neurones in the substantia nigra in the mouse, which were not reproducible in Syngenta's studies.

Gene environment interactions and pesticide toxicity, presented by **Dr Andrew Povey** (The University of Manchester, UK), focussed on the significance of genetic polymorphisms in the case of organophosphate (OP) exposure amongst sheep farmers. This presentation proceeded to describe the evidence supporting links between OP exposure and acute effects, Parkinson's Disease, developmental toxicity and chronic ill health. Andrew noted that plasma paraoxonase (PON), a key hydrolytic enzyme in metabolism of organophosphorus pesticides, exhibited ten- to forty-fold variation between individuals. The PON1 gene also exhibited genetic polymorphisms (>200 SNPs had been identified). A specific polymorphism, (Q192R) was linked to hydrolytic efficiency in vitro. However, there was only weak epidemiological association with chronic ill health in farmers who handled organophosphorus pesticides; the effect of the Q192R allele was limited to farmers who handled insecticide concentrates. More recent work has shown that PON1 status, as opposed to genotype, is more important in determining susceptibility. Furthermore, PON1 status does not provide protection against phosphorothioates diazinon and chlorpyrifos, only to the oxon forms of these compounds. Studies on knockout mice supplemented with the human form of PON1 showed no difference in susceptibility to organophosphates between Q192R allele and the wild type. The majority of epidemiological studies have found no association has been found with Parkinson's Disease and PON1 genotype; the UCLA Parkinson's Disease and Environment and Genes Study found as association with PON1 genotype only with exposed populations. Dr Povey concluded by noting that a better understanding of the interaction between genotype and metabolic activity was required, as well as a better understanding of exposure.

***Speakers (left to right) Dr. Andrew Povey, Dr. Philip Botham and Dr. Andy Smith***

In his excellent presentation, A novel approach to risk assessment of pesticides: the relevance to man of a non-cancer MoA [mode of action], **Richard Billington** (Dow AgroSciences, UK) discussed the current requirements for toxicology testing of pesticides. Using the case study of the developmental toxicity in rats of a new pesticide compound, X11422208 Richard described how the current toxicity testing system was applied. The new compound caused foetal abnormalities in rats (mainly affecting limb flexure) and neonatal pup loss (especially at the high dose level), suggesting that the compound was a teratogen, a finding which would probably have resulted in failure of registration. However, there were no such effects in rabbits, suggesting interspecies differences. An MoA programme was undertaken, which identified (through studies on phrenic nerve function and neonatal diaphragm function in the rat) that the toxicological effects in rat were due to agonism of neonatal Acetyl Choline receptor (nAChR) causing sustained muscle contraction. Subsequent investigation showed that the effect was pharmacological (due to exposure at the end of gestation) rather than teratological. Studies on the human foetal nAChR showed binding, but no agonism.

Humanised mice in the safety assessment of crop protection chemicals, presented by **Richard Currie** (Syngenta, UK), explained the current knowledge regarding used of humanised mice in toxicity testing. Firstly the definitions of different humanised animals were outlined: true humanised (in which the animal gene was replaced), transgenic (in which the human gene was added) and nude mouse plus xenograft. Points for consideration when using these animals included whether the gene was a true ortholog, inability to consider splice variants with cDNA transgenics, whether all control elements had been included and promoter issues. Richard went on to illustrate how humanised mice have been used to establish MoA and human relevance for liver tumours

observed in rodents with some crop protection chemicals. CAR/PXR humanised mice exhibited hypertrophy and hepatomegaly in response to the mouse non-genotoxic hepatocarcinogens phenobarbital and chlordane, but in the humanised mice there was no proliferation response in hepatocytes (a key mode-of-action event in liver tumour formation) whilst all three effects were observed in wild type mice. This mirrored the response seen in human primary hepatocyte cultures. Studies with CCL4 demonstrated that Car/PXR humanised mice maintained the normal proliferative response to other stimuli.

***Speakers Dr Richard Billington (left) and Dr Richard Currie***

***Symposium report by Andrew Axon***

## BTS Poster Prize winner – Andrew Axon

***Andrew is pictured here receiving his prize from BTS President Ruth Roberts at the conference dinner.***

# Special Reports

## EUROTOX 2011 Report
## Paris 28-31 August 2011

The 47th Congress of the European Societies of Toxicology 2011 was held at the Palais des Congres de Paris, France from the 28th – 31st August. The meeting was attended by over 1400 registrants from academia, industry, and government from around the world. This year's Congress was dedicated to 'Safety Evaluation: A Translational Science'. The opening Keynote Lecture was given by Prof. David Kirkland which was entitled 'From Mendel to Mutation'. Prof Kirkland gave an informative lecture on some history of in vitro genetic toxicology assays and how improvements are being made in this area. This was followed by the presentation of the Eurotox Merit Award to Dr. Gerhard Nohynek of L'Oreal, France.

There were many symposia, workshops and oral session to attend over the next few days, with a range of subjects such as genotoxicity, omics and reproductive toxicology. Monday's session was opened with a Keynote Lecture given by Prof. Gary Williams followed by an interesting symposium titled 'Evaluating potential adverse epigenetic effects of chemicals: possibilities and pitfalls'. Prof Jay Goodman gave an introduction to the topic which was followed by various speakers giving their opinion on proposed models that could be used for evaluating epigenetic effects. Dr. Richard Meehan of MRC Human Genetics Unit, Edinburgh discussed DNA methylation and a transgenic model currently being generated. Dr. Robert Feil of University of Montpellier followed on from that with a talk on genomic imprinting, and toxicological and environmental effects have on the epigenome, including alcohol consumption during gestation. Prof. Lorraine Young from The University of Nottingham followed this with an overview of stem cells and their use in environment-epigenetics assessment and Dr. Jonathan Moggs of Novartis closed the session with a talk on integrating transcriptomics and epigenomics.

Tuesday's lunchtime session provided us with the SOT/Eurotox debate entitled 'Biomarkers from blood and urine will replace traditional histopathological evaluation to determine adverse responses'. Dr. Ina Schuppe Koistinen (Eurotox) was for the motion discussing the KIM 1 as a more specific and sensitive marker of renal failure over traditional methods of evaluation and CK18 and HMGB1 as more useful marker of DILI over ALT. Prof. Kim Boekelheide (SOT) was against the motion, and in his opinion nothing could replace the historical significance of traditional histopathological techniques. He discussed the failure of prostate specific antigen as a marker of prostate cancer and its limitations in comparison to biopsy. After rebuttals from both sides

and questions the audience decided that Prof. Boekelheide presented a more convincing argument. The conference also had a huge volume of posters presented over two days on a variety of topics such as clinical toxicology, biomarkers, in vitro toxicology and food safety. There were many exceptional posters presented by academia, industry and regulatory bodies. Of course the congress was also well attended by many exhibitors, informing the attending delegates about their new and exciting products!

Finally, I was very lucky to attend this interesting and informative conference, which clearly demonstrated how the large body of work being carried out to progress many areas of toxicology.

***Emma M Large***
***University of Strathclyde***

## Scottish Toxicology Interest Group Meeting

## 15 June 2011 Medical Chirurgical Centre, Foresthill Aberdeen

The Scottish Toxicology Interest Group (STIG), now in its 5th year, held their second meeting of 2011 on 15 June in Aberdeen. The meeting was organised by Gabrielle Hawksworth and Heather Wallace, from the University of Aberdeen and included a wide range of interesting presentations. Colin Henderson (University of Dundee) began the oral presentations by discussing the need for novel humanised models in which to perform pharmacokinetic studies and highlighted a variety of murine transgenic models where key aspects of drug metabolism had been humanised. Related to this topic, John Bial (Yecuris Corporation) reported on an alternative method for humanising animal models whereby mice were manipulated to accept transplanted primary human cells. Keith Thompson (University of Aberdeen) reported on aminobisphosphate-induced γδ T-cell cytotoxicity and Frank Wood (University of Aberdeen) presented information on the action of Ipilimumab, a potential monoclonal antibody therapy for metastatic melanoma, potentiating anti-tumour T cell responses. Zoe Riches (University of Aberdeen) discussed the role of renal transporters in the nephrotoxicity of antiviral drugs while Nimesh Mody (University of Aberdeen) reported on fenretinide's ability to inhibit obesity and insulin resistance in mice. Craig Robinson provided the final talk of the day delivering insights into the environmental monitoring and (eco)toxicology carried out at Marine Scotland Science.

The poster presentations afforded attendees the opportunity to network and enjoy the light refreshments provided. Congratulations go to Rui Tarquete (University of Aberdeen) for winning the student poster presentation prize. I would like to thank the organisers and all the presenters for making this a successful, motivating and informative meeting.

For more information contact Dr Eva Malone, STIG Co-ordinator, Edinburgh Napier University (e.malone@napier.ac.uk).

***Eva Malone, Edinburgh Napier University***

## BTS Sponsored Student Report on studies by Andrew Axon, Newcastle University

Primary biliary cirrhosis (PBC) is a chronic cholestatic liver disease common in postmenopausal women, characterised by the presence of antimitochondrial antibodies. Exposure to environmental xenobiotics and estrogenic drugs has been linked to an increased incidence of PBC. It is feasible that exposure to environmental xenoestrogens may be a risk factor for PBC.

By screening a range of xenobiotics for their ability to activate the human estrogen receptors in vitro, the commonly used azo dyes, sunset yellow and tartrazine, were identified as having transcriptional estrogenic. These compounds did not however, test positive in the classical mouse uterotrophic assay. Further investigations suggested that both compounds might have a higher affinity and/or specificity for ERβ, which may not be critical for sexual development and therefore potentially explain the finings of the in vivo assay. Both sunset yellow and tartrazine caused a significant decrease in TMRM localization and sunset yellow caused a reduction in MTS reduction in primary rat hepatocytes, suggesting these compounds have a detrimental effect on mitochondrial function.

In a mouse model of chronic exposure, tartrazine was found to significantly increase portal tract inflammation (PTI), collagen deposition and increase serum ALP activity, all of which are biomarkers of cholestatic liver injury. SYBR-Green qRT-PCR analysis revealed that both estrogen and tartrazine cause significant changes in the expression MRP 1-6 and other drug/bile salt transport proteins in the mouse liver, indicating a potential mechanism for the observed cholestasis. The expression of hepatic 3a11 was inhibited in this model implying antagonism of the pregnane X receptor. These findings suggest that exposure to tartrazine, or other xenoestrogens may cause ERβ activation and PXR antagonism in the liver, resulting in altered transporter expression and a cholestatic injury. If this liver insult was coupled with damage/alteration to mitochondrial reductase enzyme function, and other genetic/environmental factors, it may be an initiating factor in PBC.

As the recipient of a PhD scholarship, funded by the BTS, UK Health Protection Agency and Medical

Toxicology Centre at Newcastle University commencing in 2008 I embarked on this research project with the specific aim of obtaining a PhD. Whilst that initial goal has remained my primary focus for the last 3 years it has been enhanced by vast amount of unexpected personal and professional gains. I have dramatically developed my communication, project management and problem solving abilities and whilst it is in the nature of scientific research to be difficult at times, I have learnt a lot about my mental toughness and resilience which I'm sure will stand me in good stead for the future.

I would like to thank the BTS, along with the other contributors for the amazing opportunity to undertake this project. I would also like to thank my supervisory team, Prof. Matt Wright, Prof. Faith Williams and Prof. Peter Blain for your support and encouragement, without which this would have been impossible. Thank you.

***Andrew Axon, Newcastle University***

## Amy Mercer

### Gordon Gibson Memorial Travel Fellowship Award 2011 recipient

Amy presenting her poster at the Gordon Conference

At the BTS Annual Congress in Durham this year I was extremely grateful to receive the first Gordon Gibson Memorial Travel Fellowship to attend the Gordon Conference of Cellular and Molecular Mechanisms of Toxicity, which was held in New Hampshire in August 2011. I am currently a post-doctoral research fellow working at the MRC Centre for Drug Safety Science (CDSS), University of Liverpool. Here my research is focussed upon defining the fundamental chemical and molecular mechanisms of drug-induced cell death the application of this mechanistic understanding to improve drug safety. Therefore attending the highly prestigious Gordon conference where I was able to present my work on the mechanisms of cell death induced by the Artemisinin family of antimalarials to an audience of international scientists was a fantastic opportunity.

This year's conference was entitled "Understanding Innovative Mechanistic Toxicology in the Post-Genomic Era" and was chaired by Ruth Roberts. The program that was put together by the organising committee was designed to interest an audience of toxicologists with a wide variety of scientific backgrounds. The success of the program was proven by the enthusiastic and enjoyable discussions generated during the sessions. The program was particularly enjoyable because of the variety of speakers presenting, with speakers from regulatory affairs, academia and industry ranging from graduate students to world leading investigators, which gave an amazing scope to the research perspectives presented.

The conference opened on Sunday evening with key note speaker Linda Birnbaum, who gave the opening session describing advances in the science of environmental health which gave a historical view of the subject right through to the most current cutting–edge advances. This was followed by the second keynote session given by Michel Karin who described the important interplay between inflammation and obesity in liver carcinogenesis. The sessions over the next week covered the very latest hot-topics in toxicology starting with sessions on the adaptive and compensatory responses to liver injury and epigenomics. The epigenomic session was a particular highlight of the meeting with exciting talks from Dana Dolinoy (University of Michigan), Shuk-mei Ho (University of Cincinnati) and David Williams (Oregon State University) describing the revolutionary findings of this field to the area of human toxicology. Tuesday saw sessions describing the important subject of the use of models and modelling to the toxiciology field. In the morning new experimental models in toxicology were described by Jon Essex (University of Southampton), who presented the use of computational models, and Aaron Bowman (Vanderbilt University Medical Centre), who presented upon the topic of patient-derived stem cells as a translational model. This was followed in the evening by three talks describing the emerging role of computational toxicology, specifically the application of in vitro pathways to in vivo models (Rusty Thomas, Hamner Institute) and the use of in silico models and high throughput screening (Richard Judson, US EPA). Wednesday saw the discussion of the interesting and significant topic, circadian rhythms in toxicology. Kristin Eckel-Mahan (UCI) and Marian Antoch (Roswell Park Cancer Institute) described the affect of circadian rhythms in the area of the hepatic metabolome and in mechanisms of stress response. A highlight of this session was a highly interesting presentation on the

unusual topic of the effect of pesticides on circadian behaviour in honey bees, selected from the breaking abstracts, delivered by Louisa Hooven (Oregon State). Wednesday evening saw a change of topic with a session addressing the pharmacogenetics and pharmacogenomics of adverse drug reactions. Munir Pirmohamed (University of Liverpool) gave an interesting perspective of the genetic determinants of idiosyncratic drug reactions and the exciting clinical implications of such studies. Ivan Rusyn (University of N. Carolina) presented on the how the use of functional genomics and systems biology can help to understand drug toxicity, and finally Ahmed Enayetallah (Pfizer) gave an industrial insight in the use of genetics and genomics in drug screening. The final day saw a switch to neurotoxicity with a morning session on the cellular and molecular mechanisms of neuroinflammation which included presentations upon the imaging of glial cell activation in vivo, from Tomas Guilarte (Columbia University) followed by a presentation by Jean Harry (NIEHS) on the related topic of the role of microglial heterogeneity in neuroinflammation and neurotoxicity. The final session of the conference, the keynote lecture, was delivered by Tim Greenamyre (University of Pittsburgh). Professor Greenamyre presented a highly original and entertaining account of his research examining the links between pesticide poisoning and Parkinson's disease which was illustrated by the first filmographic evidence of rotenone poisoning in the classic movie "The creature from the black lagoon"! This mixture of originality, excellent science and enjoyment exemplified the meeting as a whole and was a perfect way to end the conference.

Alongside these formal scientific sessions the conference provided many excellent chances to speak to other scientists informally during the afternoon sessions which were set aside for four excellent afternoon poster sessions and during the varied activity program which took full advantage of the amazing New Hampshire surroundings with biking, hiking and lake trips all included. An excellent standard of research was on show during the poster sessions which illustrated the breadth and scope of the modern toxicology field with over seventy posters displayed. These sessions were a wonderful opportunity to make new scientific connections and to discuss new ideas and were extremely well attended. I would therefore like to thank the BTS once more for the opportunity to attend the Gordon Conference of Toxicology made possible by the Gordon Gibson Travelling Fellowship. I had a wonderful time learning about many of the advances and new topics in the toxicology field and discussing my research with many fellow scientists and I will definitely hope to attend again.


Participants of the Gordon Research Conference on Cellular and Molecular Mechanisms of Toxicity August 7-12, 2011

***Written by Amy Mercer, University of Liverpool***

## MRC ITTP Training Programme July 2011

Twenty- two students funded by the MRC PhD Integrative Training Partnership (ITTP) attended the third yearly course at the MRC Toxicology Unit, Leicester University, from the 11-15th July. For the last two days the meeting transferred to Barnsdale Lodge Hotel in Rutland where besides further lectures students presented their own work in talks or posters to some of the lecturers and supervisors. The BTS president Professor Ruth Roberts gave the Keynote lecture to inspire all students in their future careers and Professor Gay Hawksworth gave her first after dinner speech. The organizers are very grateful for the input and time of the lecturers from all communities of toxicology who contributed to the week.

***Prof Andy Smith, MRC Toxicology Centre***

***ITTP students at Barnsdale Lodge, July 2011 (courtesy of Muhammad Farooq)***

# Feature Article

## An Interview with Prof Ian Kimber, OBE

Ian Kimber, one of the United Kingdom's leading toxicologists, and a long standing and well known member of our Society, was awarded the OBE for services to science in the 2011 Queen's Birthday Honours List. He kindly agreed to talk to us about his achievements, current research interests, and the challenge of refinement and replacement of animals in toxicity testing.

Ian Kimber is currently Professor of Toxicology and Associate Dean for Business Development in the Faculty of Life Sciences at the University of Manchester. Ian started his career in academia before moving into the private sector; he worked at the Central Toxicology Laboratory which was initially a part of ICI and later Zeneca, AstraZeneca and Syngenta, before moving to Manchester in 2007. He is well known for his work on the development and validation of the mouse Local Lymph Node Assay (LLNA), a method that has become an internationally-accepted regulatory standard for the identification of skin sensitising chemicals. However, Prof Kimber's research interests embrace many aspects of immunotoxicology and allergy. "Current research includes characterising the features that confer on proteins the ability to induce immune and allergic responses, the mechanistic bases for the induction of skin and respiratory sensitisation by chemicals, the roles played by Langerhans cells and other cutaneous dendritic cells in the orchestration of immune and allergic responses in the skin, the development and evaluation of novel approaches to the identification and characterisation of chemical and protein allergens, and the immunobiology of psoriasis." Prof Kimber told us. These research interests are supported by significant collaborations with industrial partners including AstraZeneca, Novartis, Johnson Matthey, BASF, Procter & Gamble and Unilever, as well as other academic centres. Ian's research group is also associated closely with the MRC Centre for Drug Safety Science. He is a firm believer in academic-industrial collaboration: "Such collaborations have always been, and remain today, a vital of component of the research strategy in our own laboratory. In recent years I have worked closely with the MRC in seeking to align more effectively the research supported with the Council with the interests and needs of industry; and in pursuing that agenda I think we have met with some success. But for all kinds of reasons the time is now right to for ensuring an ever closer association between academia and industry."

Prof Kimber is also the current Chairman of the Board of the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs). "This is a real privilege. I have a long-standing interest in the development of alternative methods and the NC3Rs is perfectly placed to align the 3Rs agenda in experimental research with the best of science and technology. The NC3Rs does fabulous work driving excellence in 3Rs science through a variety of funding schemes, and combining that with innovative Centre-led activities." Prof Kimber hailed the progress being made in this field and noted that this continues to be supported by a substantial investment in the design and development of alternative methods. "In some areas - and for the purposes of acute toxicity testing - non-animal methods are already available. The much bigger challenge is going to be developing strategies for assessing - with confidence - the potential of chemicals to cause adverse health effects following repeated systemic exposure. However, even if full alternatives for certain aspects of safety assessment remain a distant goal, there are nevertheless exciting opportunities to exploit advances in the biomedical sciences to reduce and refine the ways in which animals are used for toxicity testing, and in some areas to obviate the need for animals altogether." Despite this considerable commitment of time and resources, there was still no validated non-animal alternative to the LLNA, although Prof Kimber believes that hazard identification (is it a sensitizer or not?) should be possible relatively soon without recourse to animal testing. The much more difficult hurdle will be to find alternative strategies for hazard characterisation and determining the relative potency of skin sensitising chemicals for the purposes of risk assessment. "Potency is of course an essential consideration in all forms of safety assessment, but this is particularly important in this instance because we are aware that contact allergens vary by up to 5 orders of magnitude with respect to their relative skin sensitising potential."

Professor Kimber has published over 550 research papers, review articles and book chapters and serves currently on the editorial boards of many toxicology, immunology, dermatology and pathology journals. His prizes and other awards include the SmithKline Beecham Laboratory Animal Welfare Prize in 2000 (jointly with David Basketter and Frank Gerberick), the 9th Robert A Scala Award in Toxicology (2001), Society of Toxicology Enhancement of Animal Welfare Award in 2003 (jointly with Frank Gerberick), and the Society of Toxicology Immunotoxicology Career Achievement Award (2005). In 2010 Professor Kimber received the Bo Holmstedt Memorial Fellowship Award and Lecture at the International Congress of Toxicology. The award of the OBE this year is a fitting public recognition for his invaluable contribution to toxicological and immunological science. All of us at the BTS offer Ian our hearty congratulations.

# Discovery Toxicology

## Metabolic Profiling Methods and Protocols; Springer Protocols – Methods in Molecular Biology 693

Edited by Thomas O Metz. Humana Press, 2011. ISBN: 978-1-61737-984-0; 391 pp; £99 (hardback)

The term, 'metabolic profiling', at least as far as my memory serves me, was once years ago considered jargon and its use was frowned upon, at least by the purists. I am pleased to say that 'metabolic profiling' has now entered mainstream language and perhaps inevitably so, as it is a simple term that perfectly describes what it is. Put simply, biological samples are analysed using chromatographic methods to reveal the pattern (or profile) of metabolites contained therein. Quantification of those metabolites, although an important issue, is not always as straightforward as it might seem and the elucidation of the their chemical structural identity can sometimes be quite challenging. That's the practical side but what's the purpose of metabolic profiling? The technique can be applied to an understanding of drug metabolism, the investigation of metabolic disease and inborn errors in metabolism, through to biomarker investigations as signs of chemical toxicity. Metabolic Profiling as book covers all aspects, the what, the why and the how. It was the sort of book that this reviewer started to read and then, at least at times, found it hard to put down. Anyone (and I mean anyone) in the field should have this on their bookshelf. I will correct that statement – on their bookshelf and in the laboratory. It is the sort of book that is going to get soiled with laboratory reagents and be proud of it.

The book starts with a historical account of the subject and even contains a number of photographs of instrumentation that rather embarrassingly I recognised only too well. There then follows a series of chapters, all with the same general format, providing a general introduction and background to the subject followed by practical guides and examples, almost in the form of Standard Operating Procedures. It is this balance of a knowledge base and practicality that impressed me the most. (The editor should also be congratulated on being able to get chapters written in a consistent format, from such a wide variety of contributors).

The chapters include profiling techniques for amino acids, organic acids, purines and pyrimidines, related to inborn errors of metabolism. A range of biochemical pathways are covered such as the citric acid cycle and then a chapter on metabolite profiling relating to drug development. The latter chapter includes aspects of isotopic labelling and advantages to quantification. Following this the direction changes somewhat towards the instrumentation used in metabolic profiling such as GC-MS, LC-MS techniques, NMR and other methods. It even has a chapter on GC-MS, a technique that many bioanalytical laboratories seem to have forgotten. Overall, a well laid out practical guide and a mine of information.

Graham Lappin
Xceleron, UK

## Bioinformatics for Omics Data: Methods and Protocols; Springer Protocols – Methods in Molecular Biology 719

Edited by Bernd Mayer. Human Press, 2011. ISBN: 978-1-61779-026-3; 584 pp; £112.50 (hardback)

Bioinformatics for omics data is a whistle-stop tour of state of the art analysis techniques for the most common omics (high throughput) technologies. It covers everything from fundamental considerations for choosing a technology, through analysis pipelines for individual techniques, to highly sophisticated integrated approaches, aimed at deconvolving large, independent datasets.

Part one is designed to create a foundation for the reader in order that they might appreciate the general complexities in handling omics data. Here, the practical issues/hardware considerations are illustrated, as well as the importance of good data management policies. The book then leads on to the unusual statistical considerations that omics technologies present, with examples (namely the situations where the number of variables far exceed the number of samples). Finally, part one finishes with an illuminating chapter that firmly grounds the reader in reality about the limitations of omics technologies. For researchers who may be considering a large number of omics experiments, this is essential reading.

One of the most difficult decisions for an omics researcher is choosing an appropriate analysis methodology in the face of a proliferation of technologies that have emerged for every major omics field. Part two is focussed on providing a pragmatic foothold for researchers as they come to terms with the vast literature associated with specific technologies. These include copy number variation, ChIP-chip, transcriptomic approaches, and Mass-Spectrometry. Generally, the advice is high quality throughout, although there is a clear disparity in what can be confidently said about the biases in well studied microarray based technologies versus what is known about the biases in their next generation equivalents. For example, the authors have wisely not overplayed the significance of RNA-Seq, a technology which is evolving rapidly and thus would almost certainly lead to out of date information only a few months after publication. Nevertheless, this section remains an important introduction to these areas for non-bioinformaticians looking to speak the language of omics analysis.

The final section of the book, part three, is a biology focused set of chapters which delivers real world examples of analysis pipelines. Here, the emphasis is very much on practical methodologies to understand

and interpret the output of omics experiments, with particular attention paid to pathway/network analysis techniques. It is this final section that is most likely to be of practical value to toxicologists, as it gives some excellent examples of how to move beyond simple low level gene by gene approaches into the complex statistical analysis that will make the most of the data a researcher has generated. In addition, there is a special focus on integrating genomics, transcriptomics and proteomics outputs, along with how researchers can mine public domain data to assist in validation and hypothesis generation. The high level examples are well written and easy to follow. That said, there is a fair amount of chapter to chapter repetition on general bioinformatics concepts already covered in earlier chapters, that would have been better used to provide additional examples and/or detail of the various strengths and weaknesses of the selected techniques. This may have served to illustrate to a reader what can reasonably be expected from a serious investment in omics analysis. Finally, some specific examples of toxico-omics work would have been advantageous to toxicologists, although clearly this is not the objective of the book.

In conclusion, Bioinformatics for Omics data provides a useful introduction to the world of omics technologies without being overly prescriptive. One potential criticism is that the scope may be too wide to offer much in the way of specific assistance to a given problem, and presented as a methods book, this can seem somewhat odd at times – certainly, reading this book will not equip a reader with the instructions to carry out a detailed analysis, and any researcher engaged with the literature in an omics field will know there are usually many more facets to omics data than may first appear. However, for researchers that are looking to expand their domain knowledge into what a broad array of omics technologies can offer, this seems like a reasonable trade-off, and should provide the reader with the knowledge to engage an experienced bioinformatician with their requirements.

Richard Jackson, AstraZeneca, UK

## Tumor Models in Cancer Research, Second Edition
## Cancer Drug Discovery and Development

Edited by Beverly A Teicher. Humana Press, 2011. ISBN: 978-1-60761-967-3; 693 pp; 169.95 Euros (hardback)

Tumor Models in Cancer Research, edited by Beverly A Teicher, forms part of the Cancer Drug Discovery and Development series published by Humana Press. The book is divided into nine parts with each part comprising of between one to five chapters. Each chapter is written by an expert within that particular field of research and although individually written, the format of each chapter has for the most part been standardised with regards to its layout and content, resulting in a user friendly book. The book includes information on a range of animal models and techniques used in cancer research, focusing on their evolution, the advantages and limitations associated with them and their contribution to our understanding of cancer.

Part I (Introduction) provides a historical overview of various tumor models used in cancer research. The challenges and limitations of the assays are briefly discussed, as are the different approaches required when evaluating targeted versus cytoxic compounds.

Part II (Transplantable Syngeneic Rodent Tumors) discusses murine L1210 and P388 leukaemia models past and present and considers their role in drug development and in our understanding of tumor and host biological behaviour. A review of the B16 murine melanoma model discusses how this model has contributed to our understanding of the metastasis cascade and tumor establishment using the soil-seed theory. A chapter on syngeneic rodent tumors provides useful practical information on basic study design and data interpretation. Factors such as the importance of using high quality, homozygous animals to prevent contradictory results and the spontaneous regression of tumors, the importance of substantiating a positive response to demonstrate efficacy rather than immunological effects and the importance of having all the relevant data available before drawing conclusions are included. These points may not be ground breaking to those working within this discipline, but serve to emphasise the importance of good science in research. In Part III (Human Tumor Xenografts) xenograft models are discussed, including differences between strains of mice, the site of implantation, cells versus fragments and comparisons between subcutaneous xenograft, orthotropic xenograft and transgenic/knockout models. Other topics in this section include detailed accounts of the establishment of human tumor xenografts from patient explants, challenges associated with the Paediatric Preclinical Testing Program, the use of green and red fluorescent proteins for tracking cancer cell metastasis and an overview of imaging technologies and the end-points applied in preclinical oncology. Part IV (Carcinogen-Induced Tumors) reviews mammary cancer in rats induced by 1-methyl-1-nitrosourea and provides clear and detailed methodology for the model. Part V (Disease and Target-Specific Models) contains information on a variety of transgenic mouse xenograft models such as models of leukaemia, lymphoma melanoma and renal cell carcinoma. Animal models of mesothelioma are included in this section with the focus primarily on asbestos-induced disease and includes a review of the routes of fibre introduction, effects in different species and correlations between fibre type and length and their association with mesothelioma risk. The use of companion animals with cancer to bridge between traditional laboratory preclinical studies and the clinic concludes this section.

Part VI (Genetically Engineered Mouse Models of Cancer) reviews on the use of genetically engineered mice as models for pancreatic ductal and prostrate adenocarcinoma. The latter includes the histological and molecular characterisation of pathological progression in this model, its use in the identification of genes that regulate tumour progression and our understanding of the impact of the androgen pathway.

The final chapter in this section looks at the use of various transgenic mouse models in dietary and chemo-prevention of cancer using prostrate, mammary, intestinal and pancreatic cancer as examples. Part VII (Metastasis Models) discusses invasive and metastatic disease models and their use in the evaluation of agents directed against oncogenic signalling pathways and targeted therapies. Part VIII (Normal Tissue Response Models) discusses toxicities associated with cancer therapy and their potential to significantly reduce a patient's ability to tolerate optimal treatment. Examples of animal models, along with specific study design information are provided and include anti-neoplastic and radiation-induced mucositis, proctitis, dermatitis and osteonecrosis. Hematopoiesis and its potential role in affecting drug dose/exposure and safety margins of anti-cancer drugs are also discussed within this section. Part IX (Experimental Methods and Endpoints) is the final section in the book and includes discussions on preclinical tumor response end-points and improvements which can be made to study designs to ensure that more refined and meaningful end-points are obtained. The importance of cell survival assays to measure long term viability and the proliferative capacity of clonogenic tumour cells are discussed in relation to their role in determining the success or failure of cancer therapy. The final chapter in this book discusses imaging gene expression, physiological function and therapeutic effects in tumors using transparent window models and intravital microscopy. Details are provided for a number of procedures including chamber preparations, acute (exteriorised) preparations and in situ preparations such as the corneal pocket assay.
This book provides an overview of a wide range of animal models and techniques used in cancer research. Information is provided on how these models have evolved over time, their advantages and limitations and their contribution to cancer research. On a personal note, I would have liked to have seen a greater emphasis on how these models translate to the clinical setting and a few more examples of treatments successfully identified by using such models. A few typos here and there but nevertheless a worthy read for anyone involved or interested in the area of cancer research.

Sharon Rowton
Covance Laboratories, UK

### Chemical Carcinogenesis

Edited by Trevor M Penning. Springer, 2011. ISBN: 978-1-61737-994-9; 440 pp; £126 (hardback)

This edition of Chemical Carcinogenesis forms part of a well established series "Current Cancer Research". This edition provides a contemporary account of the advances in chemical carcinogenesis. It is a text that I would strongly recommend to anyone working within this field. This edition has kept abreast of the rapid changes in chemical carcinogenesis.
There are eighteen chapters, all of which acquaint the reader to the initiating events of chemical carcinogenesis. Each chapter is written to give the reader an overview of the individual aim of the chapter and the chapter is concluded with a clear and succinct summary. The references provided at the end of each chapter allow the reader the opportunity to follow through with further reading.
The first chapter provides an overview of chemical carcinogenesis. This chapter provides the foundations to the reason why chemical carcinogenesis is an area of such importance.

Chapters 2 to 6 provide the reader with a reminder of what is meant by multistage cancer and a series of well defined human carcinogens which illustrate how these are identified, mechanisms of action and how biomarkers are used in identification. Each carcinogen discussed also illustrates the breadth of primary targets these compounds affect. In chapters 7-11 the authors discuss using relevant examples of activation, detoxification and deamination. Chapter 12 is an interesting chapter reviewing Chemical Carcinogenesis and Epigenetics. This chapter looks at many processes we are all familiar with but deconstructs the hypotheses and reconstructs the postulate posing questions such as the involvement of methylation and the association of inflammation in cancer development. A thought provoking chapter to the discerning reader. The last chapter concentrates on the mutations and the effects on cancer development.
The text of this book allows the reader to appreciate the concepts behind chemical carcinogenesis and is supplemented with a series of well annotated diagrams and photomicrographs.

No other book of this calibre presents such a comprehensive review. And with this, I will leave you to purchase this book to formulate your own views…..

Shirley Price, University of Surrey, UK

## Risk Assessment

### Cancer Risk Assessment (Chemical Carcinogenesis, Hazard Evaluation, and Risk Quantification)

Edited by Ching-Hung Hsu and Todd Stedeford. Wiley, 2010. ISBN: 978-0-470-23822-6; 824 pp; £117 (hardback)

Cancer risk assessment is an ever-changing discipline with standard regulatory practices and defaults giving way to ever-increasing breakthroughs in scientific discovery. The scientific literature is, however, replete with reports of toxicant-induced changes, but discriminating between those reports that are irrelevant or relevant to humans and those that are compensatory versus truly adverse can be an arduous task. This book aims to inform and to provide interpretive guidance on evaluating toxicological data and understanding the relevance of such data to hazard evaluation and cancer risk estimation.

The topics included in this book start with Part I which provides an overview of cancer risk assessment,

followed by a discussion about the regulatory frameworks for industrial chemicals and biocides. The next chapter covers the general approaches for developing standards for chemicals in air, water, food, soil and consumer products. In Part II (which I would prefer to see at the beginning of Part I), basic concepts in cancer biology, chemical carcinogenesis, hormesis and experimental evidence of threshold for genotoxic carcinogens are discussed. In Part III (which is probably the most important and relevant part of this book) are discussed the testing guidelines and regulations for in vitro and in vivo genotoxicity testing. In Part IV are discussed the different interpretations and guidances regarding assessing the human relevance of chemical-induced tumours from rodent studies, along with the necessary criteria for evaluating data from epidemiological studies. In Part V covers the methods for informing cancer risk quantification, including QSAR, physiologically based pharmacokinetic modelling, "-omics", and computational toxicology. Finally, Part VI addresses general approaches for quantifying cancer risks including linear and nonlinear low-dose extrapolations, summing tumours and exposure reconstruction for cancer risk estimation.

With its focus on quantitative methods, regulation and weight of the evidence, Cancer Risk Assessment enables the readers to accurately assess human cancer risk from exposure to chemical agents, including specific examples such as solvents, metals, mixtures and nanoparticles. I am not sure this book is bringing something completely new in the field of cancer risk assessment; however it covers the main topics and could be a very good reference book for anyone embarking into cancer risk assessment.

Marc Pricivalle, Stiefel, UK

# Nanotoxicology

## Characterization of Nanoparticles Intended for Drug Delivery; Springer Protocols – Methods in Molecular Biology 697

Edited by Scott E McNeil. Humana Press, 2011. ISBN 978-1-60327-197-4; 269 pp; £85.50 (hardback)

Nanomaterials present exciting opportunities for production of complex pharmaceuticals, but also present challenges in preclinical characterisation tests. This book starts with a broad overview of applications of nanotechnology to medicine, describes some of the problems which can occur during characterisation of nanoparticle samples, and addresses some of the issues that may arise during development of a nanotherapeutic and submission for regulation. The following, and greater part of the book describes laboratory protocols for assessment of physicochemical properties, sterility, quantitation, toxicity and immunological effects of clinically relevant nanoparticles. Many of these methods have been developed and validated at the National Cancer Institute's Nanotechnology Characterisation Laboratory (NCL).

Methods are described to characterise physicochemical properties, including size, and molecular weight, zeta potential, and compositional identification of nanoparticles. Protocols are described for quantitation of free gadolinium in nanoparticle samples used as magnetic resonance imaging (MRI) contrast agents, and quantitation, of lipids in lipid-based nanoparticle formulations. Procedures are also given for preparation of ex vivo nanoparticle-containing tissue or cell culture samples for transmission electron microscopy (TEM).

In the section on sterility assays, two methods for the detection and quantification of endotoxin in nanoparticle preparations are described, one based on an end-point chromogenic limulus amoebocyte lystae (LAL) assay, and the other on measuring the turbidity of the LAL extract. A method is also included to quantitate microbial contamination of a nanoparticle formulation, using Millipore sampler devices, to avoid contamination of cell cultures and transmitting potential microbial contaminants to animals in preclinical studies.

Detection and quantitation of nanoparticles in biological samples are described, in particular, of fullerene nanoparticles in human serum, and of gold, both in solution, and taken up by macrophages. Several toxicity tests are described, with endpoints of (i) apoptosis (by quantifying caspase-3 activation in nanoparticle-treated human hepatocarcinoma cells, and (ii) autophagy (by measuring expression of the autophagosome marker LC3-II in nanoparticle-exposed porcine kidney cells (LLC-PK1)), and (iii) generation of reactive oxygen species, products of lipid peroxidation and detection of reduced and oxidised glutathione.

Several immunological assays are included in this book; using blood samples with nanoparticles, assays are described to assess their haemolytic properties, and ability to induce, or interfere with platelet aggregation. An SDS-PAGE with western blotting method is given for qualitative detection of complement activation, using C3 and cleavage products as markers for complement activation by any of the pathways (classical complement, alternative complement or lectin pathways). Cellular studies include applying an in vitro model for chemotaxis as a means of measuring the chemoattractant ability of nanoparticles, and qualitative evaluation of uptake of nanoparticles by phagocytic cells, as an adjunct to electron microscopy, confocal microscopy.

This is an excellent book for detailed guidance in methods for characterising nanoparticles for use in medicine.

Trudy L Knight
University of Birmingham, UK

## Recent Citations in Toxicology Journals sent for information from BTS members

**Baldrick P, Hewings S and Skinner M (**2011). Reproduction and juvenile animal toxicology studies in the rat with a new allergy vaccine adjuvanted with monophosphoryl lipid A (MPL®) for the treatment of grass pollen allergy. Reprod Toxicol **32(3):** 322-328

**Coggins CRE** (2010) A further review of inhalation studies with cigarette smoke and lung cancer in experimental animals, including
Transgenic mice. *Inhalation Toxicology,* ***22*****(12):** 974-983.

Gaworski CL, Oldham MJ and **Coggins CRE**. (2010) Toxicological considerations on the use of propylene glycol as a humectant
in cigarettes. *Toxicology* 269:54-66.

## Early Career Toxicologists' Sub-Committee

Careers Advice
In the past year we have promoted the Society at careers events in London, Leicester and Birmingham, which gave us the opportunity to speak to many enthusiastic university students, some of whom will hopefully go on to join the next generation of toxicologists. We're keen to attend careers events in other regions, particularly those which are targeted at biological sciences students. In the past we've also worked with university toxicology departments to hold careers talks specifically targeted at MSc students who are about to embark on their careers or PhD. If anyone knows of suitable bioscience careers events, or would like to work with us to organise careers talks, please get in touch.

We do acknowledge that times are changing; many students prefer to gather career information from the internet rather than attend a careers event. With this in mind, we've been working with the Education and Communication Subcommittees to update the Society's careers advice. Previously, this took the form of a booklet but the intention is that this should now form an integral part of the BTS website. This will allow us to reach a much wider audience of potential toxicologists. The flexibility of the format means that we can include career advice that is relevant to students at each stage of their education, from school-leavers right the way through to those who are already in post and considering how to advance their career. We're trying to find experienced toxicologists who are willing to contribute short profiles for the careers website.

**Report from the Early Career Toxicologist Sub-Committee**

As usual we're busy with this year's careers events; throughout November we've attended events in Leicester, Liverpool and York, and hope to attend events in London and Birmingham in the new year. Tom Cull, who is the link person between our Subcommittee and the Communications Subcommittee (CSC), has been working hard with the CSC to replace the increasingly dilapidated portable display unit that we use at careers events.

The revised careers advice has gone live on the new BTS website. Hopefully prospective toxicologists will find this section of the site useful. Please feel free to send us your comments and constructive feedback on this section. It could also do with some images to make the pages a little more exciting. If you have any images, or suggestions of appropriate images, please give us a shout.

The Early Career Toxicologists' Subcommittee suggested a topic for a symposium at the 2012 Annual Congress. Amy Mercer, and those working with her, have done a sterling job putting together a draft programme. I'm sure it's going to be an interesting symposium. We're also working on an improved Early Career Networking event for the Annual Congress. If all goes according to plan, we should have a separate room so early career scientists (i.e. first 10 to 15 years of their career in toxicology) can get to know each other.

David Mason
Chairman, ECT

ect@thebts.org.uk

## Register of Toxicologists – Update

Contact details for those seeking to join the Panel or other enquiries are:

The Administrator, UK Register of Toxicologists c/o Society of Biology, 9 Red Lion Court, London EC4A 3EF
Tel: +44 (0)207 936 5980 Fax: +44 (0)207 936 5901
Email: info@toxreg.org.uk Web: http://www.toxreg.org.

### New Registrants

Ms Kathryn Lynne Bibeau
Dr Meera Cush
Dr Ira W Daly
Mrs Susannah Davies
Dr Keith Stephen Dredge
Mr Edwin Efa
Dr Anne Fuchs
Dr Janis Hulla
Mrs Christine Janaitis
Prof Atholl Johnson
Dr Robert Wesley Kapp Jr
Dr Leona Merolla
Ms Malgorzata Puchnarewicz
Dr Sophie Ann Rocks
Dr Jennifer Sims
Mr Thomas Smith
Dr ClaireTerry

### Re-Registrants

Mr Peter Aughton
Dr Stephen Binks
Mr Roger Burnett
Dr Jane Collard
Mr Colin Davies
Mr David Everett
Mr Andy Gibbs
Ms Lois Haighton
Mr David Hart
Mr William Hawkins
Dr Andrew John Ingram
Dr Eian Massey
Mrs Christine McAlinden
Mr David Mitchell
Prof Michael Moore
Dr Beno Rattel
Dr Corinne van Dorp
Dr Heather Wallace

UNIVERSITY OF ABERDEEN

## MSc IN DRUG DEVELOPMENT AND DRUG SAFETY

This new course has been designed to respond to the demand for training in toxicology, with an emphasis on the assessment of drug safety. The programme aims to equip students for careers/research in the development and safety assessment of new and current drugs by providing a multi-disciplinary approach to the study of drug discovery and development; mechanisms of drug-induced toxicity; preclinical and clinical trials; regulatory affairs.

**THE PROGRAMME:**

Taught courses include

(Session 1)

**Introduction to Molecular Pharmacology, Immunology and Oncology**
**Human Drug Metabolism and Molecular Toxicology**
**Therapeutics for Scientists**
**Applied Statistics**
**Molecular Biology Basics**

(Session 2)

**Drug Development to Evidence Based Medicine**
**Pharmacokinetics and Toxicokinetics**
**Clinical Pharmacology**
**Pharmacovigilance**
**Introduction to Research Methods**

The teaching faculty includes internationally recognised experts from the pharmaceutical industry and other UK universities. Students undertake a 15 week research project – there may be opportunities to carry this out overseas.

**FUNDING:** for part costs of fees are available for UK/ EU applicants.

For further information please contact:
**Graduate School Secretariat**
**Polwarth Building**
**Foresterhill Aberdeen AB25 2ZD**
E-mail: graduateschool-clsm@abdn.ac.uk
http://www.abdn.ac.uk/clsm/graduateschool

UNIVERSITY OF BIRMINGHAM

## University of Birmingham

### Postgraduate Qualifications in Toxicology

The Masters level courses offered cover all major aspects of toxicology with a particular emphasis on the integration of molecular biology and with extensive industrial collaborations.

- **Taught MSc**: 6 taught modules and a 3 months research project.
- **PGDiploma**: 6 taught modules or 3 modules plus 3 month research project
- **PGCertificate**: 3 taught modules
- **Research based MRes**: 3 taught modules (including 1 and 3 below) plus a 6 months research project.

Research projects may be completed in academia or industry.

MSc/PGDip/PGCert may be taken part time over 2 years.

Individual modules may be attended for CPD purposes.

**Modules (5/6 weeks; suitable for secondment from Industry or Public Sector) as follows:**

| | |
|---|---|
| Sept/Oct | Metabolism and excretion of xenobiotics |
| Nov/Dec | Pharmacological, forensic and clinical aspects of toxicology |
| Jan/Feb | Molecular and cellular mechanisms of chemically-induced toxicity |
| Feb/March | Toxicology in Practice: safety assessment in industry and the environment |

**Entrance Requirements**:

MSc/PGDip/PGCert: Good honours degree.

MRes: Minimum 2.1 in a degree with a substantial molecular biology component

Funding is available for some full-time students

All Enquiries to
School of Biosciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT.
Tel: (0121) 414 5922
Email: bio-pgtadmissions@contacts.bham.ac.uk

http://www.biosciences.bham.ac.uk/study/graduate/msc/toxicology.shtml

## Newcastle University

### MRes in Toxicology

Aims

The programme provides a springboard into a career that involves a working knowledge of scientific research in academia and industry. It is designed for intercalating and fully qualified MB BS or BDS students, graduates with a BSc in the life sciences and graduates from other science disciplines. The MRes can be taken either as a stand-alone qualification or act as an entry route onto a PhD or MD.

Programme Description

The MRes is a research-based qualification with a taught component that is of an equivalent standard to an MSc. It provides training in contemporary medical and molecular biosciences through three subject-knowledge modules (60 credits), professional and key skills training (20 credits), and a 24-week laboratory-based research project (100 credits). The programme enables you to experience an internationally competitive research area, predominantly in academia but also potentially in industry. If you register for an integrated MRes/PhD, MRes/MD or MRes/DDS you will be allocated projects that are relevant to your proposed PhD or MD, or DDS programme.

Entrance Requirements

An upper-second-class Honours degree, or international equivalent, in a science or related discipline, is preferred. You should also provide two satisfactory, appropriate references.

Applicants whose first language is not English require a minimum of IELTS 6.5 (with a minimum of 6.5 both overall and for each sub-section).

Our INTO Newcastle University Centre can provide extra tuition to help you meet the University's English language requirements.

How to Apply

The MRes programmes begin at the end of September and applications are accepted at any time of year up until the closing dates. The closing date for applications from overseas students is mid-June, UK and EU graduates are encouraged to apply before the end of July. Under exceptional circumstances applications may be reviewed at the discretion of the MRes Director of Admissions and Recruitment.

For the quickest and easiest way to apply, visit our postgraduate online application site: http://www.ncl.ac.uk/postgraduate/apply/

Further Information

For further information:
UK/EU students should contact:
Medical Sciences Graduate School
Telephone: +44 (0) 191 222 7002
Fax: +44 (0)191 222 7038
E-mail: medpg-enquiries@ncl.ac.uk
www.ncl.ac.uk/biomedicine/postgrad/taught/mres/

International students wishing to discuss these opportunities may contact:
Professor Steve Yeaman
Director of International Postgraduate Studies
Faculty of Medical Sciences
Telephone: +44 (0) 191 222 7433
Email: biomed-international-pg@ncl.ac.uk

## Cranfield University

### MSc & PgDip in Toxicology and Epidemiology (Full and part-time)

**www.cranfield.ac.uk/health/tox**

See Full Page Advert for details.

Cranfield Health are also running a short course on 13-14 March 2012 , entitled Toxicology – What you need to know. Full details are available on the website:

http://www.cranfield.ac.uk/health/shortcourses/page45602.html

## Full-time MSc in Toxicology:

The University of Surrey offers a **full-time** one-year taught **Masters programme in Toxicology** (starting in September/October each year) for which scholarships are available. For further details see http://www.surrey.ac.uk/postgraduate/taught/toxicology/

This conversion programme is designed to train individuals with degrees (or other professional qualifications) in appropriate scientific disciplines for careers in all sectors of employment within toxicology, particularly in pharmaceutical, healthcare, chemical, food, agriculture, other bio-industries and regulatory agencies, or for progression to a research degree. The aim is to provide a broad appreciation of the many aspects of toxicology, with focus on the molecular mechanisms of chemically induced toxicity and the assessment of toxicological hazards.

This Masters programme at Surrey is one of the longest running in the UK, established in 1973 as a collaborative venture with industrial and government-funded toxicology departments. Since that time, over 500 students have attended the programme, with many of them now holding senior positions in toxicology all over the world. The programme continues to benefit from such collaboration with renowned toxicologists from many organisations contributing not only to teaching on the programme (~25% of the contact hours) but also to its review and development. This maximises the employment prospects of our graduates by ensuring the training is both current and relevant to industry, government and regulatory bodies.

Nine taught modules are presented over two 15 week semesters and include ~9 days of visits to toxicology establishments which form an integral part of the programme. In addition to formal lectures and syndicate work, the programme has a very strong practical element which represents over 60% of the total. Students undertake a three-month practical research project at either the University or at one of the collaborating toxicology establishments.

Toxicology research at Surrey has an international reputation. In the last Research Assessment Exercise (2008), Toxicology formed part of the submission ranked 2nd out of 63 institutions for subjects allied to medicine, building upon the maximum rating that we achieved in the previous two assessments. Hence, Toxicology research at Surrey has been independently assessed as 'world class' over the last fifteen years.

## University of Surrey

## The Modular Training Programme in Genetic Toxicology and Environmental Mutagenesis

Modifications in EU toxicology procedures and Directives such as REACH for industrial chemicals, Directive - 91/414/EEC for plant protection products (pesticides) and the recommendations of organisations such as the International Conference on Harmonisation (ICH) have increased the demand for expertise in Genetic Toxicology for both industrial and regulatory purposes.

This shortage of staff with experience and expertise in the production and assessment of mutagenicity test data led the Executive Committee of the UK Environmental Mutagen Society (UKEMS) to direct Professor Jim Parry and Dr Elizabeth Parry to develop a training programme in Genetic Toxicology and Environmental Mutagenicity Testing. This programme is now offered by the University of Surrey and aims to provide continuing education and retraining for both current and new staff in Product Safety Departments and data assessors in Regulatory Agencies.

The Modular Training Programme in Genetic Toxicology and Environmental Mutagenesis is designed to provide in-post scientists with the opportunity to obtain advanced training and a higher qualification in toxicology. This part-time programme is designed for those in full-time employment and is ideal for research managers, regulatory affairs specialists, occupational and environmental health scientists and anyone who needs to keep abreast of the developments in modern toxicology without having to enrol on a full-time training programme.

The Modular Training Programme is a part-time programme based on a series of intensive 5-day residential taught modules. The modules are preceded by distance learning. Each module comprises lectures and a variety of case studies, demonstrations/practicals, slide sessions, tutorials and syndicate work.

Completion of this programme can lead to one of the following awards from the University of Surrey:

- MSc in Genetic Toxicology & Environmental Mutagenesis
- Postgraduate Diploma in Genetic Toxicology & Environmental Mutagenesis
- Postgraduate Certificate in Genetic Toxicology & Environmental Mutagenesis

However this programme is also offered as a short course training programme for continual professional development and is accredited by the Royal College of Pathologists for Continuing Professional Development (CPD). The programme is also supported and recognised by UKEMS.

http://www.surrey.ac.uk/postgraduate/taught/genetictoxicology

# University of Surrey

## Modular training programme in Applied Toxicology:

One week short courses, with option of registering for MSc in Applied Toxicology.

The Modular Training Programme in Applied Toxicology is accredited by the Royal College of Pathologists for Continuing Professional Development

### Entrance Requirements

Applicants who wish to apply for the MSc/Postgraduate Diploma will normally possess a minimum of a science degree in a relevant subject and, in addition, will be expected to have at least one year's experience in a related area. There are no formal entrance requirements for course participants not wishing to register for the MSc/Postgraduate Diploma, although a scientific background to at least degree level is recommended.

**2011**

| | |
|---|---|
| 14-18 Nov | Biologics |
| 5-9 Dec | Principles of Experimental Toxicology and Risk Assessment(c) |

**2012**

| | |
|---|---|
| 16-20 Jan | Target Organ Toxicology – Systems II: CNS, PNS, Endocrine and Musculo-skeletal Systems(c) |
| 13-17 Feb | Immunotoxicology |
| 19-23 March | Carcinogenicity and Mutagenicity(c) |
| 16-20 April | Haematology and Clinical Biochemistry |
| 14-18 May | Toxicokinetics and Metabolism(c) |
| 4-8 June | Safety Pharmacology in Preclinical Research and Development |
| 2-6 July | Principles of Toxicological Pathology(c) |
| 10-14 Sep | Dermal Toxicology |
| 8-12 Oct | Reproductive Toxicology(c) |
| 5-9 Nov | Food Chemical Safety Evaluation |
| 3-7 Dec | Principles of Experimental Toxicology and Risk Assessment(c) |

**2013**

| | |
|---|---|
| 14-18 January | (Target Organ Toxicology – Systems III: Cardiorespiratory and Haematopoietic Systems(c) |
| 18-22 February | Design of *in vivo* Studies |
| 18-22 March | Carcinogenicity and Mutagenicity(c) |
| 15-19 April | Biomarkers |
| 13-17 May | Toxicokinetics and Metabolism(c) |
| 10-14 June | Safety Assessment of Pharmaceutical Agents |
| 8-12 July † | Target Organ Toxicology – Systems I: Liver, Kidney, Gastrointestinal Tract and Skin(c) |
| 9-13 September | Alternative Methodologies to the Use of Animals in Toxicology |
| 7-11 October | Reproductive Toxicology(c) |
| 4-8 November | Occupational Toxicology |
| 2-6 December | Principles of Experimental Toxicology and Risk Assessment(c) |

Key:

(c) denotes core module

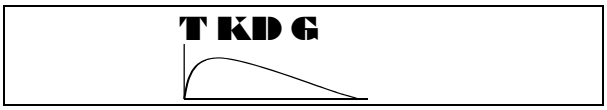
† University accommodation may be available for these dates

For further information on the above modules, or the Modular Training Programme in general, contact Professor Shirley Price, Programme Director, Modular Training Programme in Applied Toxicology. tel. 01483 689215; S.Price@surrey.ac.uk.

For further details, see http://www.surrey.ac.uk/postgraduate/taught/appliedtoxicology

## Meetings Diary

### 2012




***Toxicokinetics Discussion Group* Meeting, hosted by HLS in Cambridge 25 January 2012.**

Organising Committee:
Charlie Brindley (Chairman);
charlie.brindley@kinetassist.com
David Jones (Secretary); david.jones@mhra.gsi.gov.uk
Paul Baldrick (Scientific Coordinator);
paul.baldrick@covance.com
Peter Lawrence (Scientific Coordinator);
peter.lawrence@astrazeneca.com
Peter Fenn (Treasurer); peter.fenn@aptuit.com
Guy Healing (Scientific Coordinator);
guy.healing@astrazeneca.com

The TKDG is a forum for discussing all aspects of toxicokinetics (TK) in drug development. The following topics are under consideration:

- Clinical TK: PK at high doses including overdosing
- Phase I dose escalation beyond safety margins in clinical studies
- Potential effect of formulation/batch changes on TK
- TK and animal use in consideration of the 3 Rs
- Metabolites in safety testing (MIST) Update
- PD markers for biological drugs

Please contact anyone on the Committee if you have any ideas or would like to make a presentation or to be included in our mailing list.

*Toxicology – What you need to know, A short course at Cranfield University, Cranfield UK* 13-14 March 2012.

http://www.cranfield.ac.uk/health/shortcourses/page45602.html

**BTS Annual Congress 25-28 March 2012. University of Warwick.**

Key Themes: Nanotechnology; Drug Discovery; Inhalation Toxicology; IVTS and ITTP Symposia; Aquatic Toxicology

**Registration Opens 21st November 2011**

*SOT 51st Annual Meeting, Moscone Convention Centre, San Francisco, California* 11-15 March 2012

*48th Congress of the European Societies of Toxicology,* June 17–20, 2012, Stockholm, Sweden http://www.eurotox2012.org/

*6th International Congress of ASIATOX,* July 17–20, 2012, Sendai International Center, Sendai, Japan www.asiatox-vi.com secretariat@asiatox-vi.com

***BTS Autumn Meeting* 10-11 Sept 2012. University of Keele. For further details visit www.thebts.org**

*8CTDC Congress on Toxicology in Developing Countries*, September 10–14, 2012, Bangkok, Thailand, http://www.thaitox.org/8ctdc/

### 2013

*EUROTOX 49th Congress 2013* Sep 1-4, 2013, hosted by the Swiss Society of Toxicology, The Congress Centre, Interlaken, Switzerland http://www.eurotox2013.com

*SOT 52nd Annual Meeting* March 10-14, 2013 Henry B. Gonzalez Convention Center, San Antonio, Texas

XIII International Congress of Toxicology, June 2013 Seoul, Korea. http://www.ict2013seoul.org/

### 2014

***EUROTOX Congress 2014* hosted by The BTS 7-10 Sep 2014, Edinburgh, UK**

*SOT 53rd Annual Meeting* March 23-27, 2014 Phoenix Convention Center, Phoenix, Arizona

*XVIIth World Congress on Basic and Clinical Pharmacology* 2014. Cape Town, South Africa, July 13-18, 2014

Cranfield UNIVERSITY

# Toxicology and Epidemiology

## MSc, PgDip

## Full and part-time

Toxicology and epidemiology are two individually diverse but inter-related disciplines where there is an increasing demand for trained scientists, who have the practical skills and theoretical knowledge to operate under new EU legislation, deal with risks associated with emerging technologies and recognise how environmental conditions pose a risk to human health.

Cranfield's MSc in Toxicology and Epidemiology is a unique course in the UK and Europe in that it provides focused learning in these two intimately connected disciplines. The MSc will provide you with an understanding of the impact of chemicals, including nanoparticles on human health, the environment and integrated ecosystems, enabling you to develop comprehensive strategies to minimise the risk of future health and environmental issues.

### Focus on your career

Continued concern over environmental safety and significant changes in chemical and safety legislation have led to a demand for skilled toxicologists and epidemiologists. Our Toxicology and Epidemiology MSc has been developed to fill this demand, providing students with the skills and knowledge required to enter these complementary areas.

Graduates can expect to work in areas such as risk management/ assessment, regulatory affairs, planning and policy in a number of Government departments and agencies, pharmaceutical companies, contract research laboratories and the NHS. In addition the course will equip students with the skills needed to continue a career in academia – typically by way of a PhD programme.

The Toxicology and Epidemiology MSc is informed and updated through extensive industry-led research and consultancy activities carried out by Cranfield's Institute of Environment and Health (IEH). Their involvement means you benefit from a programme that is totally up-to-date and draws upon current developments, giving you a significant career advantage.

### Benefit from practical experience

You'll undertake a four month individual research project either in industry, with a Government partner or in academia. This is a fantastic opportunity to apply your new knowledge in a real-life setting, it also allows you to make invaluable contacts with prospective employers before even completing the degree.

As a part-time candidate, you would normally carry out the research project at your place of work in a relevant area – enabling you to make an immediate impact in your own environment.

### Skills and learning outcomes

Cranfield's MSc in Toxicology and Epidemiology will provide you with an understanding of the techniques and principles of toxicology and preclinical studies and research, epidemiology and applied statistics and analysis, risk assessment and legislation.

You will also develop a set of indispensable transferable skills.

www.cranfield.ac.uk/health/tox

## Course details

Duration: 12 months full-time.
Up to a maximum of three years part-time.

Start date: October

Entry requirements: A good honours degree from a UK university or equivalent in a relevant discipline such as biology, biochemistry, chemistry, environmental sciences or other life science-related disciplines. Candidates with appropriate professional experience wishing to develop their careers are also invited to apply.

Funding: For details of any funding that maybe available please contact the Enquiries Office.

## Contact details

For further details and application forms please contact the Enquiries Office on:

T: +44 (0)1234 758008 or
E: enquiries.health@cranfield.ac.uk

## Why Cranfield?

Cranfield University is a wholly postgraduate university with an international community and a global reputation for inspirational teaching and research, industrial-scale facilities and superior links with industry and commerce.

Students choose Cranfield for:

- new dedicated facilities as part of a £35 million University investment
- excellent employment prospects – 93% of our graduates secure relevant employment within six months of graduation
- superb academic support – we have an excellent staff-to-student ratio
- exciting personal research projects that can be carried out in industry or academia.

Course structure

- Assessed taught modules 50%
- Integrated component 10%
- Individual research project 40%

## Module outline

- Introduction to Toxicology and Epidemiology – an overview of the principles of toxicology and epidemiology with associated ethical considerations and legal guidelines.
- Research Design and Methodology – how to design, fund and manage research, plus key tools for analysis of results.
- Statistical Analysis and Interpretation – how statistical methods are used in scientific studies.
- Principles of Toxicology – toxicology studies and guidelines.
- Pre-clinical Research – exploration of the scientific research generated through preclinical studies.
- Research Governance and Ethics – the ethos, requirements and legislation surrounding human subject research.
- Basic Epidemiology and Statistics – introduction to the basic concepts and methods of epidemiology.
- Applied Epidemiology – practical application of applied epidemiology to the investigation of public health problems.
- Business Principles – how to protect and exploit your inventions.
- Risk Assessment and Regulation – the legal and risk-based regulatory framework for the management of environmental pollution and its impact on human health; development of communication strategies to manage perception of risk.

The MSc is based on ten compulsory taught modules, an integrated component and a research project and thesis. The PgDip includes ten compulsory taught modules and an integrated component. The marks for each of the modules are obtained from a piece of coursework which may take the form of a portfolio, debate, lab report or presentation. The pass mark for all components is 50%.

## Who should apply?

This course is designed for recent graduates wishing to begin a career in toxicology or epidemiology, or for those already working and looking to either enhance their careers or move into one of these fields. Available on a full and part-time basis, the course offers flexibility and support for those who wish to study whilst remaining in employment.

Course video available online

www.cranfield.ac.uk/health/tox

# rsa.
Regulatory Science
## Consultancy

**rsa.** is a first-class regulatory science consultancy business

**Established in May 2007, Regulatory Science Associates is an independent consultancy group of highly qualified and experienced specialists with backgrounds in major blue chip companies.**

We are an enthusiastic and dedicated team of reputable toxicologists, ecotoxicologists and regulatory affairs specialists.

### Our services

**General**
- **Strategy** and **planning** on techno-regulatory issues
- **Project management** including cross-functional and international teams
- **Emerging legislation** impact

**Specific Services**
- **Toxicology areas of expertise** particularly in genetic toxicology, metabolism and pharmacokinetics, neurotoxicology, oncogenicity, pathology, endocrine disruption and reprotoxicology.
- **Specific issues:** development of focused research proposals
- **Human and environmental safety**: Risk assessment, product safety and defense
- **Structural analogues:** review, interpretation and toxicity impact assessment
- **Critical assessment** of complex data, derivation of **risk assessment endpoints**

**Documentation**
- **IUCLID/OECD summary** preparation
- **Position papers**, rebuttals, waiver requests
- **Literature review**, peer review
- **Presentations** at **scientific meetings**

**Regulatory Services**
- **Product registration**, maintenance and re-registration
- **Dossier preparation**
- **Product defense**
- **Regulatory Authority**, advocacy, liaison and representation

**Study management**
- **Study protocol development**
- **Study management** including monitoring, issue resolution, critical data communication and draft report reviews

**Trust in our experience and expertise**

For more information
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e-mail info@regulatoryscience.com

**www.regulatoryscience.com**