



A Community of Practice that  
makes a difference to your work and career!

# Workshop on Predictive ADME & Toxicology

**Hands-On Practice Approach**

**Oxford University, July 27-31, 2009**

**Interactive pragmatic workshops  
with leading experts and industry  
practitioners...**

- ▶ ADME-guided Library Design
- ▶ Knowledge-based Toxicity Prediction
- ▶ Carcinogenicity Prediction
- ▶ QSAR Validation
- ▶ Regulatory Assessment Strategies
- ▶ REACH-based Hazard Assessment
- ▶ OECD Principles & Reporting Formats
- ▶ Modelling Skin Penetration, Irritation
- ▶ Predictive ADMET Workflows



**A hands-on focus to Predictive ADMET using  
leading-edge methods and software. Discuss  
practical examples, case studies and methods.**

- ▶ Class facilitation and discussions led by Community Manager Dr. Barry Hardy and an international faculty team of expert predictive ADMET application practitioners. Emphasis on collaborative work and learning.
- ▶ Use leading predictive ADMET software packages including Leadscope, Lhasa, Iazar, OECD toolbox, Tox-match, Metasite, StarDrop, DiscoveryBus.
- ▶ Integrating case study approach and group work throughout the week on methods, datasets, challenging problems and discussion of results obtained
- ▶ One year's membership of eCheminfo included



The workshops will take place at the  
Medical Sciences Teaching Center, Oxford  
University.

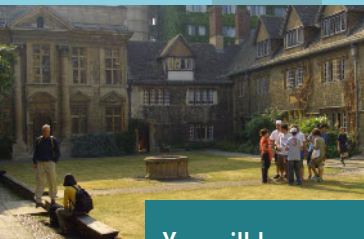


Library Design incorporating ADME Prediction and Metabolic Properties  
Ismael Zamora (Pompeu Fabra University and Lead Molecular Design)

- ▶ Practice methods for the prediction of ADME properties
- ▶ Study prediction of permeability and solubility
- ▶ Examine un-specific protein binding
- ▶ Analyse cytochrome-mediated metabolism of xenobiotics
- ▶ Analyse and discuss predictions for celecoxib
- ▶ Overcome problems that slow down lead optimization



"I took home a lot of new ideas – things I would like to try out as soon as possible to improve the support of the work of our medicinal chemists." UW, 2006



You will have ample opportunity to discuss your perspectives and criticisms of the methods studied and you'll take-away key nuggets of understanding from these intensive sessions.

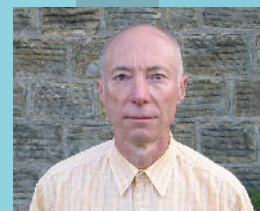


Using Database Look-ups, Read Across, and Predictive Models to assess the Toxicity of Compounds, Glenn Myatt (Leadscope)

- ▶ Use database look-ups and read across
- ▶ Develop predictive models to assess the toxicity of compounds
- ▶ Search over toxicity data including US FDA databases
- ▶ Discuss issues concerning data mining toxicity
- ▶ Finding structural alerts
- ▶ Modelling when the training data can or cannot be examined

Knowledge-based Reasoning for the Prediction of Toxicity and Metabolism, Philip Judson (Lhasa Ltd.)

- ▶ Non-statistical approaches to the prediction of toxicity and metabolism
- ▶ Knowledge-based toxicity prediction and metabolism
- ▶ Reasoning-based prediction and subjectivity in predictions
- ▶ Assessing reliability of qualitative & statistical predictions
- ▶ Judge and compare predictions from reasoning-based and statistical models



A fully equipped IT classroom and a variety of software packages will be at your disposal to work through the problems posed by the instructors.

"Great week with a very well balanced distribution of talks, hands-on tutorials and social events. All presentations very relevant and enough social activities to get the participants together to engage in discussions." WL, 2007

Lazy-Structure-Activity-Relationships (lazar) for the in-silico Prediction of Chemical Carcinogenicity, Christoph Helma (in silico toxicology)

- ▶ Develop prediction of carcinogenicity for case study dataset
- ▶ Predict for untested structures from experimental toxicities
- ▶ Provide understandable and traceable prediction rationales
- ▶ Discriminate between (un)trustworthy predictions
- ▶ Assign a confidence index to each prediction
- ▶ Carry out cross-validation experiments with various carcinogenicity and mutagenicity endpoints
- ▶ Determine predictive accuracies for structures



Modelling the "Toxicity Pathway" from Chemistry to Effect, Mark Cronin (School of Pharmacy & Chemistry, Liverpool John Moores University)

- ▶ Group chemicals together into categories reliably
- ▶ Perform read-across to make predictions of toxicity
- ▶ Form categories from structural analogues, mechanisms of toxic action, as well as chemicals with similar modes
- ▶ Apply OECD (Q)SAR Application Toolbox for structure input, data retrieval and category formation
- ▶ Apply and test categorisation approach on case study datasets

Time is set aside throughout the week to work in small groups on case study datasets.

"Excellent workshop. Informative and enjoyable from start to finish. Lots of new ideas and best practices to implement asap. It was a great group with lots of different areas of expertise. Scientists from all over the world meant that discussions were interesting and informative." NP, 2007



Return to your lab with new ideas, best practices and software experiences to maximise productivity in your own predictive ADMET activities.

QSAR Validation Criteria and Concepts, Judith Madden (School of Pharmacy and Chemistry, Liverpool John Moores University)

- ▶ Assign a confidence to a predictive approach in toxicology
- ▶ Assess robustness and accuracy of a model
- ▶ Apply OECD Principles for the Validation of (Q)SARs
- ▶ Verify, characterise, and evaluate predictive (Q)SARs
- ▶ Perform exercises based on the OECD validation criteria
- ▶ Discuss REACH endpoints and method extensions to pharma data

Application of Structure-Activity Relationships in REACH-compliant Chemical Hazard Assessment, Arianna Bassan (S-IN)

- ▶ Regulatory use of QSARs under REACH including satisfying requirements for validation, applicability domain, adequacy, and documentation
- ▶ Reporting in QSAR Model Reporting Format, QMRF
- ▶ Select approaches for predicting individual toxic endpoints
- ▶ Generate endpoint predictions and integrate results
- ▶ Document in a transparent way the use of the methods
- ▶ Apply Toxmatch tool to toxicity datasets and report results



"Plenty of diversity in topics. Excellent facilities. I did not realise how many tools were out there. The course structure was good. Social events especially punting facilitated discussion. Good contacts made. Put a lot in context. Hands-on approach a big bonus over lectures." MM, 2006

Modelling Skin Penetration, Irritation, Sensitization and Penetration Enhancement, Tony Hopfinger (University of New Mexico)

- ▶ Develop 4D-FP fingerprints for penetrants which include size, shape, chemical composition, reactive state and molecular flexibility
- ▶ Apply membrane-interaction (MI-) QSAR analysis to Skin ADMET
- ▶ Derive descriptors from transport simulation of a phospholipid membrane
- ▶ Apply methods to skin penetration, skin irritation and sensitization, and skin penetration enhancement
- ▶ Derive therapeutic indices optimizing penetration and minimizing irritation, sensitization and/or toxicity as a function of chemical structure



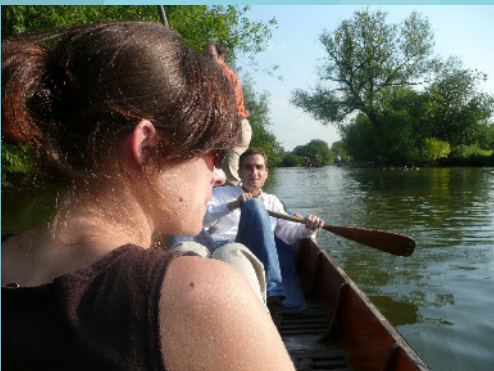
ADME QSAR Modelling to Guide Drug Design  
Olga Obrezanova (BioFocus DPI)

- ▶ Build predictive ADME models to guide drug design and synthesis
- ▶ Build a QSAR/QSPR model of properties using Gaussian Processes
- ▶ Combine *in vitro* data and *in silico* predictions to identify compounds with a balance of appropriate ADME and potency
- ▶ Use a 'probabilistic' scoring algorithm to prioritise and select compounds most likely to meet project criteria
- ▶ Use predictive model and visualisation tool to guide the redesign of compounds to overcome liabilities



Evaluation of Strengths and Weaknesses of QSAR-based Predictive ADMET Workflows, David Leahy (University of Newcastle)

- ▶ Explore both generic and local QSAR modelling methods that can be routinely updated as new data is added
- ▶ Apply best-practice QSAR modelling approaches to case studies
- ▶ Use Inkspot Science's integration platform to simplify access to chemoinformatics and statistical tools
- ▶ Evaluate the strengths and weaknesses of alternative QSAR modelling methods using the competitive workflow methods of the "Discovery Bus"



Enjoy the Oxfordshire countryside after an intensive day in the computer lab!

Join the OpenTox Open Source Development Community at [opentox.org](http://opentox.org)

The goal of the OpenTox project is to develop a predictive toxicology framework, that provides a unified access to toxicological data, (Q)SAR models and toxicological information. We welcome participation in community activities! OpenTox is supported by the EC FP7 research program.



OpenTox



## Join this international community of leading scientists...

Founded in 2003, eCheminfo is an ongoing Community of Practice (CoP) committed to the core value of outreach with diverse groups in the commercial, government and academic sectors for the sharing of best practices and the development of strategies, resources and methodologies that address specific issues in improved drug discovery and safety.

The network involves a diversity of subject matter expertise comprised of experienced professionals from the life science and pharmaceutical industry, vendors, research institutes, universities and government.

A strong emphasis on science and innovation in addition to networking and personal contacts and discussion is followed at eCheminfo events. Collaborative research projects furthering drug discovery and safety innovation goals are currently being pursued to advance the creation of a community of research approach to challenging problems and issues.

[echeminfo.com](http://echeminfo.com)

## Bursary Award

A bursary award program will be used to support the attendance of a selection of academic participants who are working in the area of predictive ADME & Toxicology.

To apply for the bursary, please send an email to eCheminfo at [douglasconnect.com](mailto:douglasconnect.com). Your application must include descriptions of your research and training needs (ca. 500 words each), and your CV. The recipients of the award will be selected based on an evaluation of the quality and innovation of the described research and the potential positive impact of the training on their research progress. See the eCheminfo website for more information including deadlines.

I felt the workshop was extremely beneficial and interesting in the sense it covered a diverse range of topics within the drug design field. It was extremely useful for determining what I would like to do in the future. The accommodation at St Edmunds was excellent and the location was perfect. Thank you for an excellent week."  
AM, 2006

## Register now for eCheminfo's Workshop Week on Predictive ADME & Toxicology

### 5 ways to register...

- ✓ Online at [echeminfo.com](http://echeminfo.com)  
(Ticket Office is only visible after login)
- ✓ Email [echeminfo at douglasconnect.com](mailto:echeminfo@douglasconnect.com)
- ✓ Phone Nicki Douglas on +41 61 851 04 61
- ✓ Fax +44 870 112 38 44 (eFax)
- ✓ Post Douglas Connect, Baermeggenweg 14  
4314 Zeiningen, Switzerland

### Please select

- I wish to register for the eCheminfo Predictive ADMET Week taking place at Oxford University 27-31 July, 2009  
Registration Fee: Regular £1500 / Academic £750
- Please contact me over local accommodation options for staying in college during the training week (subject to availability).

All registration payments must be received in advance of the Training Week.

Payments can be made by bank transfer, cheque or credit card: Amex, MasterCard, Visa

Name

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Company/institute

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Tel:

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Email:

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Billing Address

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City

Postcode

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Country

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Date

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