QSARs and REACH

A Guide to Sources of Information and Advice

PETA
PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

QSARs and REACH: Summary

Two central principles of the REACH Regulation are the promotion of alternative methods and animal testing should be a last resort. Many mechanisms are built into REACH to permit the use of alternative methods in place of animal tests. In particular, the use of Quantitative Structure Activity Relationships (QSARs) is recognised and specifically encouraged within the legal text of the REACH Regulation and the detailed REACH Guidance documents.

QSARs predict chemical behaviour directly from chemical structure and simulate adverse effects in cells, tissues and lab animals, minimising the need to use animal tests to comply with regulatory requirements for human health and eco-toxicology endpoints. REACH authorities have established principles for the appropriate use of QSARs for REACH, including within the context of weight-of-evidence arguments, which can be used to waive animal test requirements. The technology requires skilled use and expert judgement to be utilised most effectively. While QSARs are a highly valuable tool, using them inappropriately or failing to submit the resulting data appropriately may result in failure at REACH compliance check, leading to additional costs and expense and unnecessary animal testing. Used appropriately, particularly within the context of intelligent testing strategies and in combination with a chemical category approach, QSARs can provide cost-effective and timely data to help ensure REACH compliance.

The following selected resources and contacts can provide information to ensure optimal use of QSARs for REACH compliance. They have been selected exclusively on the basis of expert judgement by QSAR specialists and advocates for alternative methods, and this list is being distributed *gratis* by the animal protection charity People for the Ethical Treatment of Animals Foundation (PETA).

REACH Guidance

Practical Guide: How to Report QSARs
http://echa.europa.eu/documents/10162/17250/pg_report_qsars_en.pdf

Practical Guide: How to Report Weight of Evidence
http://echa.europa.eu/documents/10162/17250/pg_report_weight_of_evidence_en.pdf

Endpoint Specific Guidance (including Intelligent Testing Strategies and use of QSARs)
http://echa.europa.eu/documents/10162/17224/information_requirements_r7a_en.pdf

Online Resources

ECHA Read-Across Webinar
http://bit.ly/yzNOZX

OECD Toolbox
http://www.oecd.org/document/54/0,3746,en_2649_34379_42923638_1_1_1_1,00.html

OECD Toolbox (tutorial)
www.qsartoolbox.org

VEGA (includes downloadable tools)
http://www.insilico.eu/

ANTARES Project (includes list of models suitable for REACH endpoints)
http://www.antares-life.eu/

JRC (includes downloadable tools)
http://ihcp.jrc.ec.europa.eu/our_labs/computational_toxicology

OSIRIS Webtool
http://osiris.simpple.com/

Expertise and Consultancy Services

Dr Emilio Benfenati, Laboratory of Environmental Chemistry and Toxicology, Italy

LECT, based at the Istituto di Ricerche Mario Negri, has wide-ranging experience in the development of software for chemical predictive methods, including many EC-funded projects on QSAR and non-testing methods. LECT predictive models are freely available on the internet: DEMETRA, CAESAR, and the successor to CAESAR, VEGA. Dr Benfenati coordinates the working group on QSAR established by the Italian authority for REACH. LECT can develop new local QSAR models by request for specific chemical classes or use existing QSAR models for physico-chemical, fate, environmental, eco-toxicological and toxicological endpoints. On the basis of the results of the QSAR models, LECT prepares a document assessing the validity, applicability domain and reliability of the QSAR results for REACH.

Contact: benfenati@marionegri.it
Web: http://www.insilico.eu/

Bibra, UK

The 14 expert toxicologists employed at Bibra providing toxicology advice and consulting are experienced in applying various approaches to avoid new tests, including identification of existing data (using the unique Bibra toxicity databank), read-across from similar substances, interpretation of *in vitro* data, sourcing and interpretation of QSAR and SAR, and preparation of data-waiving arguments as well as weight-of-evidence approaches encompassing all relevant information. Bibra is a desk-based organisation, and all of its senior toxicologists are professionally accredited (SB/BTS and EUROTOX).

Contact: pete.watts@bibratoxadvice.co.uk
Web: www.bibra-information.co.uk

Mark Cronin, Liverpool John Moores University, UK

Mark Cronin provides consultancy and advice on undertaking predictive *in silico* toxicology, developing quantitative structure-activity relationships (QSARs) and creating categories (or grouping) of chemicals to perform read-across. He has expertise in the application of these techniques to the prediction of human health effects, environmental endpoints and physico-chemical properties. Training and educational activities on the development, use and application of QSARs and read-across are also available.

Contact: m.t.cronin@ljmu.ac.uk
Web: http://www.staff.livjm.ac.uk/phamcron/qsar/qsar1.htm

Douglas Connect, Switzerland

Douglas Connect (DC) have many years' experience in scientific research, informatics, education and marketing and have been involved in organising scientific, communication and consulting projects and solutions since 1995. Predictive toxicology services include the following:

- Preparation of REACH-relevant reporting for submission dossiers
- Preparation of QSAR models, validation and predictions
- Leading expertise with *in silico* methods, QSAR, read-across, computational chemistry
- Expertise with *in vitro* methods, analysis and expert argumentation and weight-of-evidence reporting for REACH Annex XI purposes
- Extensive network and community of leading experts

Contact: Barry.Hardy@douglasconnect.com
Web: www.douglasconnect.com

International QSAR Foundation to Reduce Animal Testing, USA

The International QSAR Foundation is primarily a research organisation promoting greater use of QSAR methods in regulatory risk assessments in order to reduce animal testing and improve margins of safety for chemical substances. It has been instrumental in the development of the QSAR Toolbox by OECD and ECHA and in the use of the categories approach to filling data gaps for untested chemicals. The Foundation specialises in extending QSAR applications to complex health endpoints, where simple statistical models are least reliable and transparent to regulators. The QSAR Foundation provides expert consultations and expert reviews for draft REACH dossiers.

Contact: gilman.veith@qsari.org
Web: www.qsari.org

Molcode, Estonia

Molcode provides a full REACH QSAR service. Using JRC reviewed and listed QSAR models, Molcode offers fully documented and REACH compliant QSAR reports for over 30 endpoints. QMRF (QSAR Model Reporting Format) and QPRF (QSAR Prediction Reporting Format) according to OECD requirements are provided including the CLP classification. Preliminary QSAR results are supplied to enable clients to assess the quality of the results and to ensure they are appropriate for the chemical registration strategy. Free training webinars on QSAR use are also provided.

Contact: mariliis@molcode.com
Web: www.reachqsar.com

REACH Monitor, Spain

REACH Monitor SLNE is a start-up company of the University of Barcelona, composed of specialists in toxicology of different areas: risk assessment, regulatory documentation, quantitative structure-activity relationships (QSARs) as well as other alternative methods for toxicity prediction. REACH Monitor has particular expertise in application of the OECD Toolbox.

Contact: info@reachmonitor.org
Web: http://www.reachmonitor.org/index.php?lang=2&aptd=0&txt=&id

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Prof Dr Gerrit Schüürmann, Umwelt Forschung Zentrum, Department of Ecological Chemistry, Germany

Dr Schüürmann gives lectures (human toxicology, eco-toxicology, environmental chemistry) and training courses with software applications (both at the UFZ and on site), focusing on REACH-relevant endpoints and non-animal methods, in particular on *in silico* (QSAR, read-across, structural alerts, application domain) and *in chemico* (chemo-assays sensing toxicity-relevant electrophilic reactivity) as well as instruction in and support of the free-of-charge OSIRIS edition of the ChemProp software that covers human and environmental toxicology endpoints and physico-chemical and fate-related properties.

Contact: gerrit.schuurmann@ufz.de
Web: http://www.ufz.de/index.php?en=1785

S-IN Soluzioni Informatiche, Italy

S-IN Soluzioni Informatiche offers complete molecular informatics services to generate *in silico* (non-testing) data in compliance with the REACH regulation.

Services

- Predictions of eco-toxicity and physico-chemical properties for regulatory use
- Assistance in generating reliable predictions by means of suitable methods and approaches
- Training in underlying methodologies, interpretation of results, and use of appropriate software

S-IN can count on a sound knowledge of tools, methodology and underlying principles for profiling chemical hazards by means of non-testing methods. S-IN offers support for using diverse *in silico* approaches as valuable components of the regulatory assessment strategy.

Contact: info@s-in.it
Web: http://www.s-in.it/en/reach.php

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People for the Ethical Treatment of Animals (PETA) Foundation (also known as PETA UK) is the UK-based affiliate of PETA US, which has more than 3 million members and supporters. PETA US and PETA UK scientists and policy experts collaborate on projects addressing regulatory testing issues at the international level, working with corporate and government entities to develop and implement non-animal testing methods. PETA welcomes contacts with companies, regulators and all other stakeholders with an interest in reducing and replacing animal experimentation. The resources listed in this document are not comprehensive, and further information and links to resources are available on request. We welcome feedback from REACH registrants and their representatives about this document and their experience of using QSAR for this purpose.

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