



## New models to assess developmental toxicity for REACH

**In line with EU legislative requirements, new research has developed models to assess the toxicity of chemicals in terms of their effects on human development. One of the models has been made freely accessible online, so that it is easy to use for industry and regulators.**

**The EU legislation REACH<sup>1</sup>** (Registration, Evaluation and Authorization of Chemicals) requires the assessment of the toxicity of a large number of chemicals. Developmental toxicity is receiving increasing attention and refers to any effects that interfere with the normal human development, such as reduced childhood growth, death and defects of foetuses and embryos. However, developmental toxicity is extremely complex and expensive to test, so is one of the most difficult types of toxicity to assess.

As part of the EU CAESAR<sup>2</sup> project, researchers developed QSAR (Quantitative Structure-Activity Relationship) models to assess the developmental toxicity of chemicals. A QSAR model attempts to find consistent relationships between the molecular properties and the biological activity of a series of chemical compounds (the 'training set') so that "rules" can be identified to evaluate new chemicals. For the method to work efficiently, the selected compounds in the training set should be a diverse range of chemicals.

The quality of any QSAR model depends on the quality of the data on chemicals. Therefore the research used a collection of good quality data that was the largest available when the project started.

The models demonstrated a good level of accuracy in their predictions of developmental toxicity and were an improvement on previous models based on the same data. However, the models also need to be easy to use. A workshop with regulatory stakeholders and industry representatives established the features that would make the models usable, and the researchers developed a free web-based application that allows the user to submit a list of compounds for which toxicity is known, execute the model and obtain developmental toxicity results for new compounds. One of the QSAR models was inserted into this on-line platform.

An important aspect for interpreting results from QSAR models is the so-called 'applicability domain', which is an evaluation of the model's suitability for reliably predicting compounds. This is also a requirement of REACH.

The CAESAR platform for the QSAR models allowed the user to evaluate the suitability of the model using three approaches. The first explores any 'problems' with the training set as a whole by, for example, checking the range of molecular descriptions of the compounds. The second assesses the similarity of six compounds in the set to the submitted chemical, and the third evaluates the model's prediction errors of these six compounds. Using these three approaches increased the reliability of the model and satisfies the requirements of REACH. It also guides the user towards safe application of the model.

**Additional information:** The free model for assessing developmental toxicity is available to download from: [www.caesar-project.eu/software/#QMRF](http://www.caesar-project.eu/software/#QMRF)

1. See [http://ec.europa.eu/environment/chemicals/reach/reach\\_intro.htm](http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm)
2. CEASAR (Computer Assisted Evaluation of Industrial Chemical Substances According to Regulations) was supported by the European Commission under the Sixth Framework Programme. See: [www.caesar-project.eu](http://www.caesar-project.eu)

**Source:** Cassano, A., Manganaro, A., Martin, T. *et al.* (2010) CAESAR models for developmental toxicity. *Chemistry Central Journal*. 4(Suppl 1):S4. This article is free to view at: [www.journal.chemistrycentral.com/content/4/S1/S4](http://www.journal.chemistrycentral.com/content/4/S1/S4)

**Contact:** [emilo.benfenati@marionegri.it](mailto:emilo.benfenati@marionegri.it)

**Theme(s):** Chemicals, Risk assessment

The contents and views included in Science for Environment Policy are based on independent, peer-reviewed research and do not necessarily reflect the position of the European Commission.

To cite this article/service: "Science for Environment Policy": European Commission DG Environment News Alert Service, edited by SCU, The University of the West of England, Bristol.