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Workshop Proceedings
QSAR Toolbox Workshop

The workshop on the use of the QSAR Toolbox was held at ECHA on 24 November 2011. This report reflects the discussions and feedback users of the Toolbox gave.

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Workshop on the use of the OECD QSAR Toolbox - Feedback from industry users and development needs

The workshop on the "Use of the QSAR Toolbox – Feedback from Industry Users and Development needs" - was held at ECHA on 24 November 2011. This report reflects the discussions and feedback users of the Toolbox gave. This feedback is considered important input for ECHA and the OECD, in the defining, prioritisation of further developments and promotion of the Tool.

The objectives of the workshop were:

- Sharing experience and best practice in the use of the QSAR Toolbox
- Identifying needs for the implementation of additional features in the QSAR Toolbox
- Identifying needs for other types of support in view of the next registration deadline 2013

The OECD secretariat presented the general principles of the QSAR Toolbox for use in read-across and grouping of chemicals approaches including the long term objectives and the future plans for developments.

The two main sessions of the workshop ('Grouping of Chemicals, ITS and AOP approaches' and 'Technical Features and Usability') included presentations from the QSAR Toolbox users, which covered how the software has been used so far for data gap filling and within ITS strategies as well as conceptual and technical needs for further development.

A summary of the main points from the discussion during the workshop is presented below.

USE OF THE QSAR TOOLBOX FOR REACH PURPOSES

The QSAR Toolbox is seen as a very practical help for registrants in the preparation of registration dossiers, but it cannot replace expert judgment. It is an expert tool, and an adequate understanding of both the tool and the scientific principles is needed before it can be used appropriately.

The QSAR Toolbox is identified as having a much wider application than its use for REACH registration purposes. It is for instance considered an important tool for innovation in the sense that it helps in the identification of potential low hazardous candidates in product development.

It was recognised that QSAR approaches were used by users to more often address information requirements for less complex (eco)toxicological endpoints and usually in a qualitative way to support the choice of the experimental point of departure. For more complex endpoints testing or waiving has so far been preferred.

QSARs were also used as supporting information to substantiate studies of less than ideal quality as part of WoE approaches or to provide more justification for waivers (e.g.

environmental fate) or as a means of substantiating the context of similarity for an endpoint as part of a category approach. In particular, QSAR approaches were employed by users to address information requirements for physicochemical properties and aquatic toxicity and used as supporting information for environmental fate and mammalian toxicity.

It was also mentioned that addressing the need to have legitimate possession of data brings challenges, which have not yet been solved.

One main challenge identified is the use of the read-across approach for experimental studies that are only now proposed and where the experimental data are not yet available.
Some participants indicated that so far the preference for registration purposes was given to the analogue approach rather than the category approach for practical reasons and the repetition of the same study records across different registration dossiers was also identified as a problem.

The read-across and data gap filling was mostly done by addressing similarity on the basis of common functional groups and breakdown products.

With regard to how the QSAR Toolbox allows addressing similarity between analogues based on common breakdown products, there is a need to address which are the critical metabolites and their incorporation in the QSAR Toolbox together with the parent compounds to allow comparative profiling and data gap filling. The use of metabolic profilers is considered sufficient for screening purposes but may not be adequate for the full coverage of regulatory needs.
The Adverse Outcome Pathways concept is considered useful for the future use of the QSAR Toolbox for data gap filling and ITS strategies. More communication during developments in this area is needed between the OECD Secretariat and the QSAR Toolbox users.

Some preference is given to endpoint specific, data gap filling with practical challenges of deriving categories of larger sizes mainly due to costs in relation to data access.

Participants expressed an interest in having REACH Categories (as submitted by registrants) available in the QSAR Toolbox and indicated that it would also be useful if the QSAR Toolbox could provide information on other existing regulatory submissions of Categories (e.g. OECD HPV programme, U.S EPA).

The use of the QSAR Toolbox for the data gap filling of UVCB substances is currently considered to be limited. More work on enabling the generation of representative structures for this class of compounds is considered beneficial. It was also noted that variability in the composition of UVCBs is carried over in the experimental data.

Adequate and reliable documentation for category and analogue reporting formats is considered a very manual exercise that is nor currently facilitated by either IUCLID or the QSAR Toolbox when preparing registration dossiers for REACH.

QSAR TOOLBOX FUNCTIONALITIES

The new features in the current version of the QSAR Toolbox are considered very useful by the users. The available tutorial files (slides) are very important and users consider their update essential for each new version of the application released.

Interest was expressed in having a better understanding of the data coverage in the Tool, for instance knowing how much of the CAS registry is covered by the inventories/databases included in the QSAR Toolbox.

Participants also expressed an interest in the identification of new databases for inclusion in the QSAR Toolbox (e.g. Flavouring groups from EFSA).

The need for setting-up an open plug-in framework to enable the docking of third party modules in the QSAR Toolbox in order to extend its functionality was also reported by participants. Potential functionalities that might be docked-in were i.e. more specific metabolism simulators, additional profilers, additional predictors and links to external QSAR tools.

The profilers are considered useful but improvement of the description of the fields and background information for each profiler is seen as essential.

The project team will continue to explore the possibility of enabling the transfer of local databases between local installations of the software.

Additional help functionalities (online help) to enhance user friendliness as well as the identification of options for reporting errors and new information directly from the QSAR Toolbox are considered very important for the future development of the application.

Other areas suggested for improvement in the future versions of the application include:

- Possibility to enable creation of macros for some very frequent actions
- Possibility for exchanging the predictions in saved QSAR Toolbox projects
- Batch mode (processing list of chemicals)
- Displaying the quality of relation of CAS numbers, name and Smiles should be more intuitive
- Plug-in functionalities to other tools for import of output would be favoured but the need for adequate planning was stressed
- Import/export function from IUCLID 5.3 to the QSAR Toolbox.
- Data Exchange with eChemPortal and the possibility to exchange bigger datasets between users/databases
- Need for new and flexible ontology in the QSAR Toolbox to enable good mapping with IUCLID databases and addition of users' import needs of data/information
- Ensure all endpoints from IUCLID templates (e.g. flashpoint, physical state) are also included in the QSAR Toolbox list of endpoints
- Restoring the default option for tree hierarchy view option
- There is no history record available but reporting formats can be used instead

CONCLUDING REMARKS AND WAY FORWARD

Participants indicated that the QSAR Toolbox has been very useful for the preparation of the first registration deadline, and more users foresee its potential use for the preparation of registration dossiers for the 2013 and 2018 registration deadlines.

It was highlighted that future developments within the QSAR Toolbox project (e.g. AOP approach) could be of benefit for the 2018 deadline.

The workshop participants reminded of the need for further promotion of OECD Harmonised Templates for reporting data/information by different projects to enable use of data in the QSAR Toolbox and avoid new databases with new formats.

Participants also pointed out the need for establishing an open docking framework to extend Toolbox functionality. Such a framework should be well documented to allow the development of additional modules by third party developers.

The participants indicated that they would like to participate in the testing of the use of REACH 2010 Data, once it is made available in the QSAR Toolbox.

The participants expressed the need for additional focused Guidance for the justifications in relation to data gap filling for REACH purposes for the next deadlines. It was mentioned that better communication between ECHA and Registrants is also needed in this area.

It was stressed that it would be very useful to have more information including new functionalities of the QSAR Toolbox via Webinars or presentations available at the QSAR Toolbox website with new releases. This type of information flow would be best facilitated by ECHA, OECD Secretariat and BIAC to ensure that the information reaches a wider audience, including SMEs.

It was also identified that there is a need to improve/expand existing user manuals to include a detailed description of functionalities that are not very clear to the users.

Additional suggestions were:

- Investigate how to improve the structure of the existing QSAR Toolbox Discussion Forum (https://community.oecd.org/community/toolbox_forum) to serve reporting of problems.
- To consider other ways/events for the promotion of non-test methods and QSAR Toolbox use.
- Global communication via simple means (ICCA/GPS) and links to case studies when the ECHA newsletter with the QSAR Toolbox Workshop article is published and other fora (e.g. ECETOC Task Forces).