



(Q)SAR APPLICATION TOOLBOX

VERSION 1.1

TIPS AND TRICKS

October 2009

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FOREWORD

This document is one of a series of guidance documents accompanying the OECD (Q)SAR Application Toolbox. The main objective of the Toolbox is to allow the user to use (Q)SAR methodologies to group chemicals into categories and to fill data gaps by read-across, trend analysis and (Q)SARs. For in-depth background information on the concept of chemical categories, the user is invited to consult the guidance document for grouping of chemicals published in the Series on Testing and Assessment of the OECD Environment, Health and Safety Publications [OECD (2007); ENV/JM/MONO(2007)28: [http://apli1.oecd.org/olis/2007doc.nsf/linkto/env-jm-mono\(2007\)28](http://apli1.oecd.org/olis/2007doc.nsf/linkto/env-jm-mono(2007)28)].

The current document is aimed at providing some guidance on some advanced features for using the Toolbox. It will be updated and expanded as further guidance becomes available.

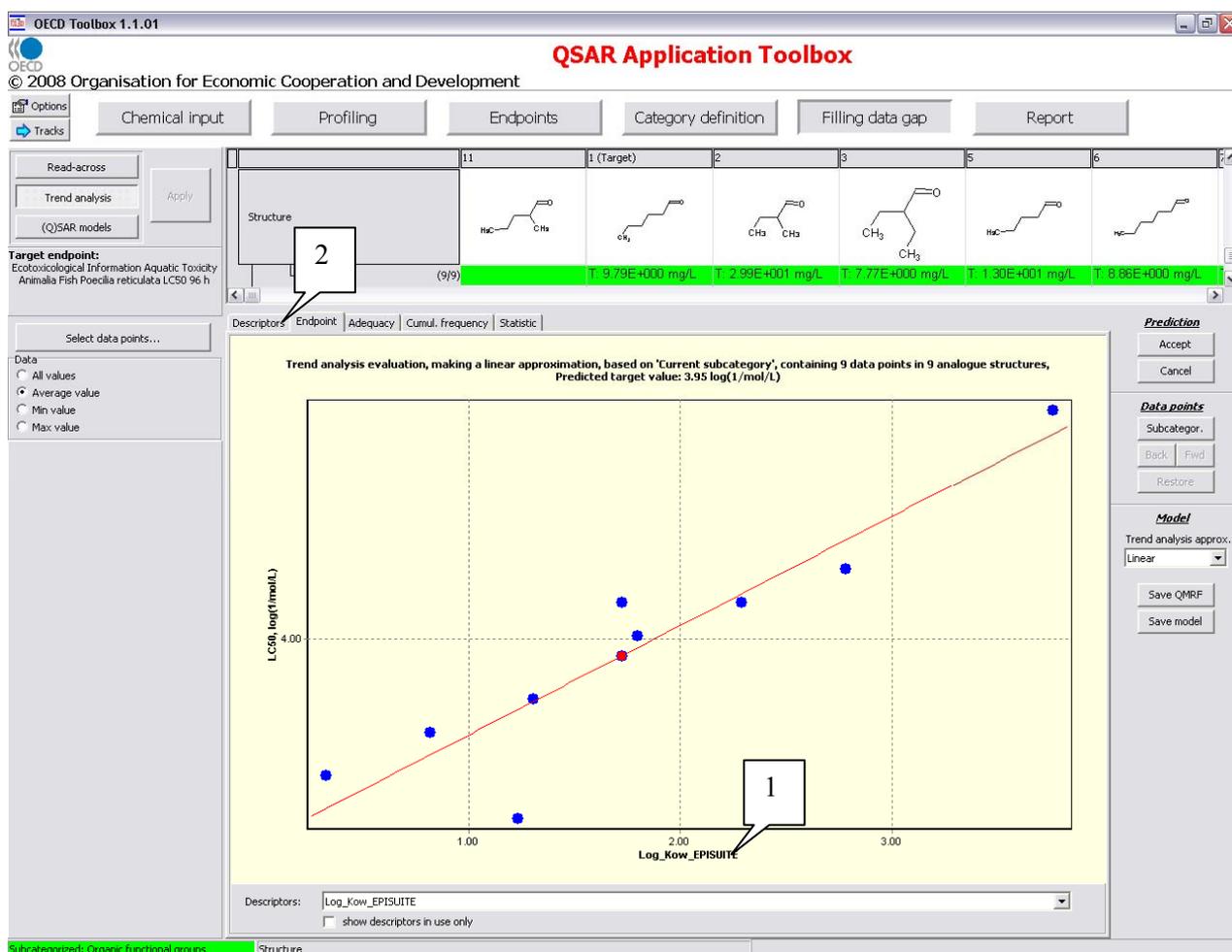
Additional guidance and training material will be made available on the internet site for the OECD (Q)SAR Project [www.oecd.org/env/existingchemicals/qsar] as well as the internet site of the Laboratory of Mathematical Chemistry [<http://toolbox.oasis-lmc.org/>] and the user is invited to regularly consult these two internet sites.

The OECD (Q)SAR Application Toolbox has been developed with the financial assistance of the European Union.

1. CHANGING THE X-AXIS DESCRIPTOR WHEN PERFORMING TREND ANALYSIS WITH THE TOOLBOX.

When performing a trend analysis within a category to estimate missing data with the Toolbox, the default X-axis descriptor is Log_Kow_EPISUITE, i.e the Log Kow estimated with the EPISUITE program (1) [see screenshot below]. While this descriptor may be pertinent for many endpoints, e.g. aquatic toxicity, alternative descriptors may be warranted for other endpoints (e.g. vapour pressure for acute inhalation toxicity).

It is possible to change the descriptor and re-estimate the property. For that the user has to select the tab **Descriptor** (2)



Among the available descriptors the user then has to select the desired descriptor (1) and click the button **Add** (2).

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QSAR Application Toolbox

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Options | Tracks | Chemical input | Profiling | Endpoints | Category definition | Filling data gap | Report

Read-across | Trend analysis | (Q)SAR models | Apply

Target endpoint:
Ecotoxicological Information Aquatic Toxicity
Animals Fish Poecilia reticulata LC50 96 h

Structure

11	1 (Target)	2	3	5	6	
96 h	(9/9)	T: 9.79E+000 mg/L	T: 2.99E+001 mg/L	T: 7.77E+000 mg/L	T: 1.30E+001 mg/L	T: 8.86E+000 mg/L

Select data points...

Data:
 All values
 Average value
 Min value
 Max value

Descriptors | Endpoint | Adequacy | Cumul. frequency | Statistic

Available descriptors:

Name	Units	Data points	Correlation (R)	Info
Henrys LC_expDB_EPISUITE	atm-m3/mole	N/A	N/A	Henrys LC (exp database)
HIA_Multicase	%	N/A	N/A	Human Intestinal Absorption - [%]
Ka_HalfLife_pH_7_EPISUITE	Days	N/A	N/A	Ka Half-Life at pH 7
Ka_HalfLife_pH_8_EPISUITE	Days	N/A	N/A	Ka Half-Life at pH 8
Kb_HalfLife_pH_7_EPISUITE	Days	N/A	N/A	Kb Half-Life at pH 7
Kb_HalfLife_pH_8_EPISUITE	Days	N/A	N/A	Kb Half-Life at pH 8
Kp_EPISUITE	m/s	N/A	N/A	Permeability coefficient from water
log PCF	log(l/kg wet)	N/A	N/A	OASIS Model 1
log BCF max	log(L/kg wet)	N/A	N/A	OASIS Model 2
Log_Kow_Exp_EPISUITE	N/A	N/A	N/A	Log Octanol-Water Partition Coef (SRC)(Exper. database match)
logP_Multicase	9	0.912		Log(Octanol/Water)
Max Diam	Å	N/A	N/A	OASIS
Max Distance	Å	N/A	N/A	OASIS
Max Donor Delocalizability	(a.u)2/eV	N/A	N/A	MOPAC 7 QCPE
Melting_Pt_EPISUITE	°C	N/A	N/A	Melting Pt (deg C)
Min Diam	Å	N/A	N/A	OASIS
MP_expDB_EPISUITE	°C	N/A	N/A	Melting Pt (exp database)
MW	Da	9	0.919	Molecular mass
Number of aromatic bonds	N/A	N/A	N/A	OASIS
Number of cyclic bonds	N/A	N/A	N/A	OASIS
Number of double bonds	N/A	N/A	N/A	OASIS
Number of rings	N/A	N/A	N/A	OASIS
Number of single bonds	N/A	N/A	N/A	OASIS
OH_HalfLife_CisIsomer_EPI...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Cis-isomer]
OH_HalfLife_TransIsomer...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Trans-isomer]
OH_Rate_Const_CisIsomer...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Cis-isomer]
OH_Rate_Const_TransIsom...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Trans-isomer]
Ozone_HalfLife_CisIsomer...	Hrs (12-hr ...	N/A	N/A	Ozone Reaction, Half-Life [Cis-isomer]

Descriptors in use:

Name	Units	Data points	Correlation (R)	Info
Log_Kow_EPISUITE		9	0.924	Log Octanol-Water Partition Coef (SRC)

Subcategorized: Organic functional groups

Prediction: Accept, Cancel

Data points: Subcategor., Back, Fwd, Restore

Model: Trend analysis approx.: Linear, Save QMRF, Save model

1 (points to Log_Kow_Exp_EPISUITE in available descriptors table)

2 (points to Add button)

The correlation is then calculated for the new descriptor and added into the window **Descriptors in use** (1)

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Options | Tracks | Chemical input | Profiling | Endpoints | Category definition | Filling data gap | Report

Read-across | Trend analysis | (Q)SAR models | Apply

Target endpoint:
Ecotoxicological Information Aquatic Toxicity
Animula Fish Poecilia reticulata LC50 96 h

Select data points...

Data:
 All values
 Average value
 Min value
 Max value

Structure	11	1 (Target)	2	3	5	6
	(9/9)	T: 9.79E+000 mg/L	T: 2.99E+001 mg/L	T: 7.77E+000 mg/L	T: 1.30E+001 mg/L	T: 8.86E+000 mg/L

Descriptors | Endpoint | Adequacy | Cumul. frequency | Statistic

Available descriptors:

Name	Units	Data points	Correlation (R)	Info
Max Donor Detocalizability	(a.u)2/eV	N/A	N/A	MOPAC 7 QCFE
Melting_Pt_EPISUITE	°C	N/A	N/A	Melting Pt (deg C)
Min Diam	Å	N/A	N/A	OASIS
MP_expDB_EPISUITE	°C	N/A	N/A	Melting Pt (exp database)
Number of aromatic bonds		N/A	N/A	OASIS
Number of cyclic bonds		N/A	N/A	OASIS
Number of double bonds		N/A	N/A	OASIS
Number of rings		N/A	N/A	OASIS
Number of single bonds		N/A	N/A	OASIS
OH_HalfLife_CisIzomer_EPI...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Cis-isomer]
OH_HalfLife_TransIzomer_...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Trans-isomer]
OH_Rate_Const_CisIzomer_...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Cis-isomer]
OH_Rate_Const_TransIzo...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Trans-isomer]
Ozone_HalfLife_CisIzomer_...	Hrs (12-hr ...	N/A	N/A	Ozone Reaction, Half-Life [Cis-isomer]
Ozone_HalfLife_TransIzom...	Hrs (12-hr ...	N/A	N/A	Ozone Reaction, Half-Life [Trans-isomer]
Ozone_Rate_Const_CisIzo...	cm3/molecu...	N/A	N/A	Ozone Reaction, Ozone Rate Constant [Cis]
Ozone_Rate_Const_TransI...	cm3/molecu...	N/A	N/A	Ozone Reaction, Ozone Rate Constant [Trans]
Planarity		N/A	N/A	OASIS
Soil_Adsorption_Coeff_KO...		N/A	N/A	Soil Adsorption Coefficient KOC
Soil_Adsorption_Coeff_Log...		N/A	N/A	Soil Adsorption Coefficient LogKOC
Subcooled_liquid_VP_EPISU...	log(1/mm Hg)	N/A	N/A	Subcooled liquid VP
Total_biodegradation_EPIS...	%	N/A	N/A	Removal In Wastewater Treatment, Total biodegradation
Total_Ka_EPISUITE	L/mol-sec	N/A	N/A	Total Ka (acid-catalyzed) at 25 deg C
Total_Kb_EPISUITE	L/mol-sec	N/A	N/A	Total Kb for pH > 8 at 25 deg C
Total_removal_EPISUITE	%	N/A	N/A	Removal In Wastewater Treatment, Total removal
Total_sludge_adsorption_E...	%	N/A	N/A	Removal In Wastewater Treatment, Total sludge adsorption
Total_to_Air_EPISUITE	%	N/A	N/A	Removal In Wastewater Treatment, Total to Air
Van D. Waals Sur.	Å2	N/A	N/A	OASIS

Descriptors in use:

Name	Units	Data points	Correlation (R)	Info
Log_Kow_EPISUITE		9	0.924	Log Octanol-Water Partition Coef (SRC)
MW	Da	9	0.919	Molecular mass

Subcategorized: Organic functional groups | Structure

Prediction: Accept, Cancel

Data points: Subcategor., Back, Fwd, Restore

Model: Trend analysis approx.: Linear, Save QMRF, Save model

1

The user can then simply delete the previous descriptor in use by selecting it (1) and clicking **Remove** (2).

Target endpoint:
Ecotoxicological Information Aquatic Toxicity
Animala Fish Poecilia reticulata LC50 96 h

Structure	11	1 (Target)	2	3	5	6
<chem>CC(=O)C</chem>						
	96 h (9/9)	T: 9.79E+000 mg/L	T: 2.99E+001 mg/L	T: 7.77E+000 mg/L	T: 1.30E+001 mg/L	T: 8.66E+000 mg/L

Available descriptors:

Name	Units	Data points	Correlation (R)	Info
Max Donor Decalizability	(a.u)2/eV	N/A	N/A	MOPAC 7 QCPE
Melting_pt_EPISUITE	>C	N/A	N/A	Melting Pt (deg C)
Min Diam	A	N/A	N/A	OASIS
MP_expDB_EPISUITE	>C	N/A	N/A	Melting Pt (exp database)
Number of aromatic bonds		N/A	N/A	OASIS
Number of cyclic bonds		N/A	N/A	OASIS
Number of double bonds		N/A	N/A	OASIS
Number of rings		N/A	N/A	OASIS
Number of single bonds		N/A	N/A	OASIS
OH_HalfLife_CisIzomer_EPI...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Cis-isomer]
OH_HalfLife_TransIzomer_...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Trans-isomer]
OH_Rate_Const_CisIzomer...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Cis-isomer]
OH_Rate_Const_TransIzom...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Trans-isomer]
Ozone_halfLife_CisIzomer...	Hrs (12-hr ...	N/A	N/A	Ozone Reaction, Half-Life [Cis-isomer]
Ozone_halfLife_TransIzom...	Hrs (12-hr ...	N/A	N/A	Ozone Reaction, Half-Life [Trans-isomer]
Ozone_Rate_Const_CisIzo...	cm3/molecu...	N/A	N/A	Ozone Reaction, Ozone Rate Constant [Cis]
Ozone_Rate_Const_TransI...	cm3/molecu...	N/A	N/A	Ozone Reaction, Ozone Rate Constant [Trans]
Planarity		N/A	N/A	OASIS
Soil_Adsorption_Coeff_KO...		N/A	N/A	Soil Adsorption Coefficient KOC
Soil_Adsorption_Coeff_Log...		N/A	N/A	Soil Adsorption Coefficient LogKOC
Subcooled_liquid_VP_EPISU...	log(1/mm Hg)	N/A	N/A	Subcooled liquid VP
Total_biodegradation_EPIS...	%	N/A	N/A	Removal In Wastewater Treatment, Total biodegradation
Total_Ka_EPISUITE	L/mol-sec	N/A	N/A	Total Ka (acid-catalyzed) at 25 deg C
Total_Kb_EPISUITE	L/mol-sec	N/A	N/A	Total Kb for pH > 8 at 25 deg C
Total_removal_EPISUITE	%	N/A	N/A	Removal In Wastewater Treatment, Total removal
Total_sludge_adsorption_E...	%	N/A	N/A	Removal In Wastewater Treatment, Total sludge adsorption
Total_to_Air_EPISUITE	%	N/A	N/A	Removal In Wastewater Treatment, Total to Air
Van D. Waals Sur.		N/A	N/A	OASIS

Descriptors in use:

Name	Units	Data points	Correlation (R)	Info
log_kow_EPISUITE		9	0.924	Log Octanol-Water Partibion Coef (SRC)
MW	Da	9	0.919	Molecular mass

By selecting the tab **Endpoint** (1) the graph with the new interpolation appears.

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Options | Tracks

Chemical input | Profiling | **Endpoints** | Category definition | Filling data gap | Report

Structure	11	1 (Target)	2	3	5	6
	(9/9)	T: 9.79E+000 mg/L	T: 2.99E+001 mg/L	T: 7.77E+000 mg/L	T: 1.30E+001 mg/L	T: 8.66E+000 mg/L

Target endpoint:
Ecotoxicological Information Aquatic Toxicity
Animalia Fish Poecilia reticulata LC50 96 h

Select data points...

Data:
 All values
 Average value
 Min value
 Max value

Descriptors: Endpoint | Adequacy | Cumul. frequency | Statistic

Trend analysis evaluation, making a linear approximation, based on 'Current subcategory', containing 9 data points in 9 analogue structures, Predicted target value: 3.97 log(1/mol/L)

Descriptors: show descriptors in use only

Subcategorized: Organic functional groups

Prediction
Accept | Cancel

Data points
Subcategor. | Back | Fwd | Restore

Model
Trend analysis approx.: Linear
Save QMRF | Save model

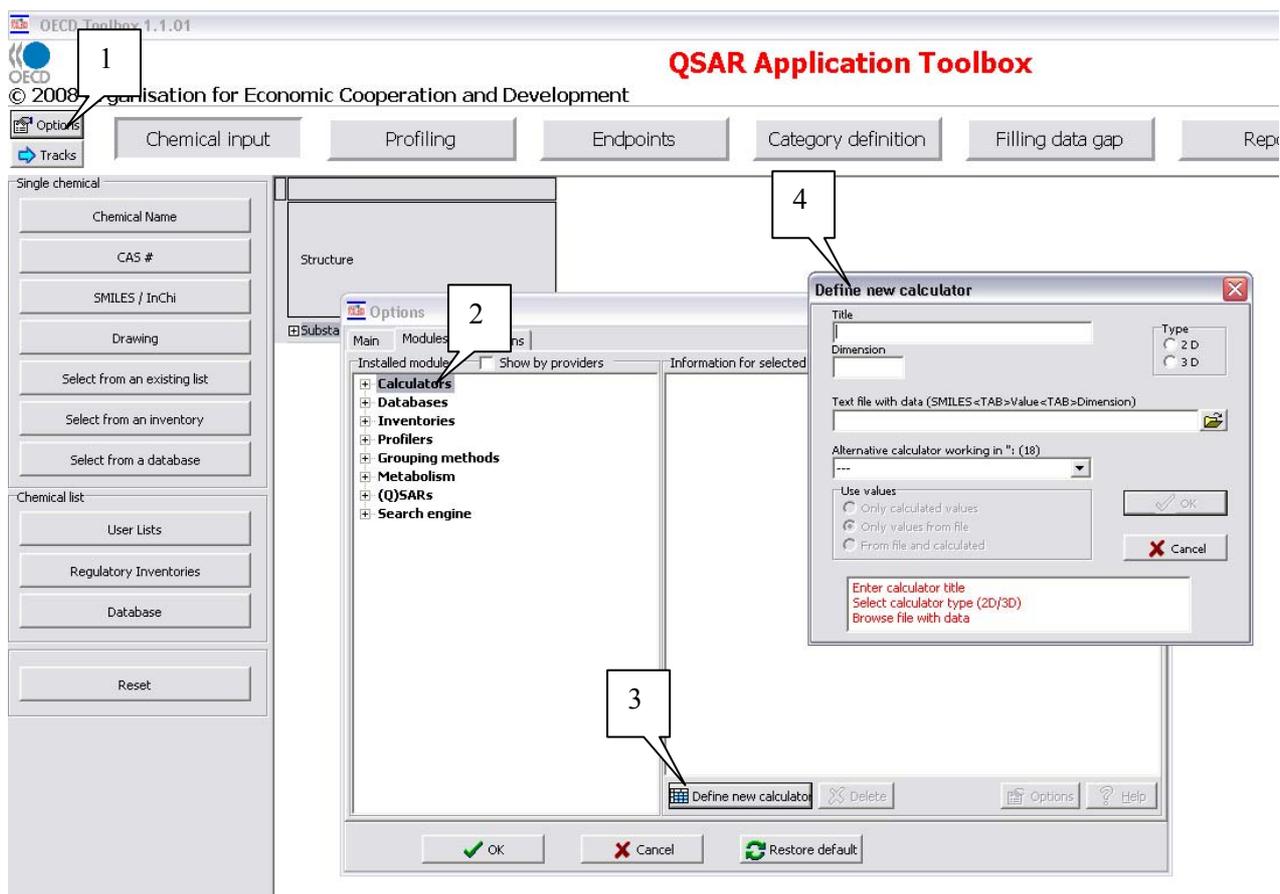
2. USING EXPERIMENTAL RESULTS FOR THE X-AXIS DESCRIPTOR

When performing trend-analysis and read-across, a number of X-axis descriptors can be used (see chapter

1. Changing the X-axis descriptor when performing trend analysis with the Toolbox.). Most of these descriptors are derived by calculation e.g. Log Kow from the KowWin module in EPISUITE.

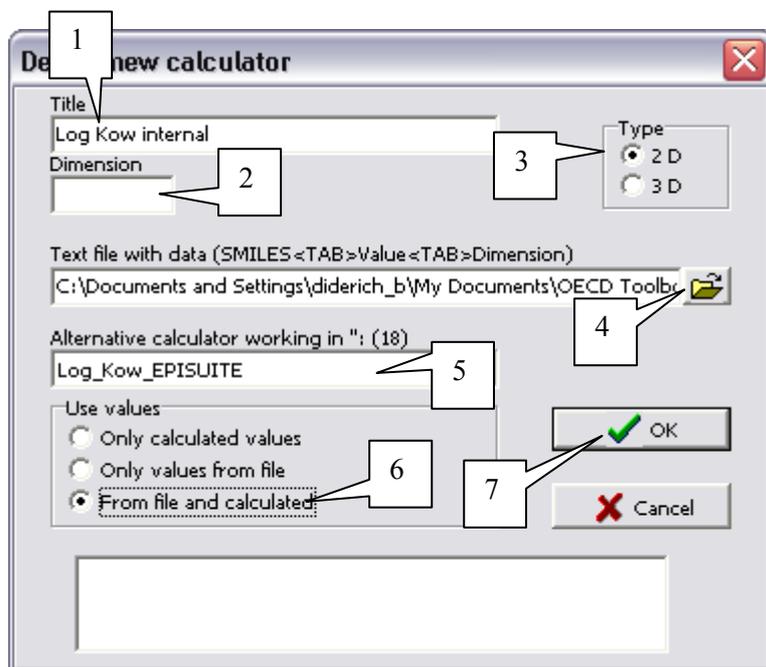
In addition to using those calculators, the user has the possibility to load datasets with experimental data to be used instead of the estimated descriptors. This is illustrated with an example below of loading a database with experimental Log Kow results.

New X-axis descriptors can be added via the module **Options** (1) [see screenshot below]. In the new window, the user then has to select the item **Calculators** (2) and click the button **Define new calculator** (3). This opens a third window dedicated to providing details of the new descriptor (4).



To define the new descriptor, the following steps should be followed (see also screenshot below):

1. Add a title. In this example "Log Kow internal"
2. Add a dimension or unit. In this example the descriptor is dimensionless and the field is left blank.
3. Select a type: 2D or 3D. The distinction is made depending on whether the descriptor could be calculated based on a 2D or 3D configuration of the structure. Kow being usually derived from a 2D structure, the 2D button can be selected.
4. Indicate the path of the file containing the Log Kow results. The file should be a normal tab delineated text file, each line having the format: SMILES<TAB>Value<TAB>Dimension. Please note that in case the descriptor is dimensionless, each line should nevertheless contain a <TAB> after the Value an example of a text file is presented in Box 1.
5. The user can choose an existing calculator to estimate the descriptor for chemicals not listed in the file with experimental data. In this example, the EPISUITE model could be chosen to fill data gaps in the experimental file.
6. Please note that if an alternative calculator is chosen, the radio button **From file and calculated** has to be checked.
7. By clicking the **OK** button, the file is imported as a new descriptor. And the user can return to a normal work session.



Box 1. Format of a text file with experimental results

C(C)S <TAB> 1.4 <TAB>

C(S)CCCC <TAB> 3.3 <TAB>

C(S)CCCCCCC <TAB> 4.3 <TAB>

Notes:

- There should be no title line and no empty line at the bottom of the file (i.e. no "Carriage Return" at the end of the last line).
- The file has to be saved with a TXT extension (e.g. Log_KOW_internal.txt).

When performing a trend analysis or read-across the new descriptor appears in the list (see screenshot below), and can be used as an X-axis descriptor as outlined in chapter 1 of this guidance document.

Available descriptors:

Name	Units	Data points	Correlation (R)	Info
Kb_HalfLife_pH_8_EPISUITE	Days	N/A	N/A	Kb Half-Life at pH 8
Kp_EPISUITE	n/s	N/A	N/A	Permeability coefficient from water
log BCF	log(L/kg wet)	N/A	N/A	OASIS Model 1
log BCF max	log(L/kg wet)	N/A	N/A	OASIS Model 2
Log Kow internal		3	0.978	
Log_Kow_Exp_EPISUITE		N/A	N/A	Log Octanol-Water Partition Coef (SRC)(Exper. database match)
logP_Multicase		N/A	N/A	Log(Octanol/Water)
Max Diam	A	N/A	N/A	OASIS
Max Distance	A	N/A	N/A	OASIS
Max Donor Dealkalibility	(a.u)2/eV	N/A	N/A	MOPAC 7 QCPE
Melting_Pt_EPISUITE	°C	N/A	N/A	Melting Pt (deg C)
Min Diam	A	N/A	N/A	OASIS
MP_expDB_EPISUITE	°C	N/A	N/A	Melting Pt (exp database)
MW	Da	N/A	N/A	Molecular mass
Number of aromatic bonds		N/A	N/A	OASIS
Number of cyclic bonds		N/A	N/A	OASIS
Number of double bonds		N/A	N/A	OASIS
Number of rings		N/A	N/A	OASIS
Number of single bonds		N/A	N/A	OASIS
OH_HalfLife_CisZomer_EPI...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Cis-isomer]
OH_HalfLife_Transzomer...	Hrs (12-hr ...	N/A	N/A	Hydroxyl Radicals Reaction, Half-Life [Trans-isomer]
OH_Rate_Const_CisZomer...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Cis-isomer]
OH_Rate_Const_Transizo...	cm3/molecu...	N/A	N/A	Hydroxyl Radicals Reaction, OH Rate Constant [Trans-isomer]
Ozone_HalfLife_CisZomer...	Hrs (12-hr ...	N/A	N/A	Ozone Reaction, Half-Life [Cis-isomer]
Ozone_HalfLife_Transzom...	Hrs (12-hr ...	N/A	N/A	Ozone Reaction, Half-Life [Trans-isomer]
Ozone_Rate_Const_CisZoz...	cm3/molecu...	N/A	N/A	Ozone Reaction, Ozone Rate Constant [Cis]
Ozone_Rate_Const_Transi...	cm3/molecu...	N/A	N/A	Ozone Reaction, Ozone Rate Constant [Trans]
Planarity		N/A	N/A	OASIS
Soil_Adsorption_Coeff_KO...		N/A	N/A	Soil Adsorption Coefficient KOC

Descriptors in use:

Name	Units	Data points	Correlation (R)	Info
Log_Kow_EPISUITE		3	0.981	Log Octanol-Water Partition Coef (SRC)