

# The CONCERT Gateway

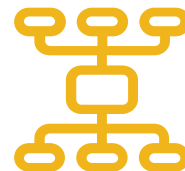
EU LIFE CONCERT REACH final workshop  
Milan, 19 June 2023

Nelly Giuseppa Raitano

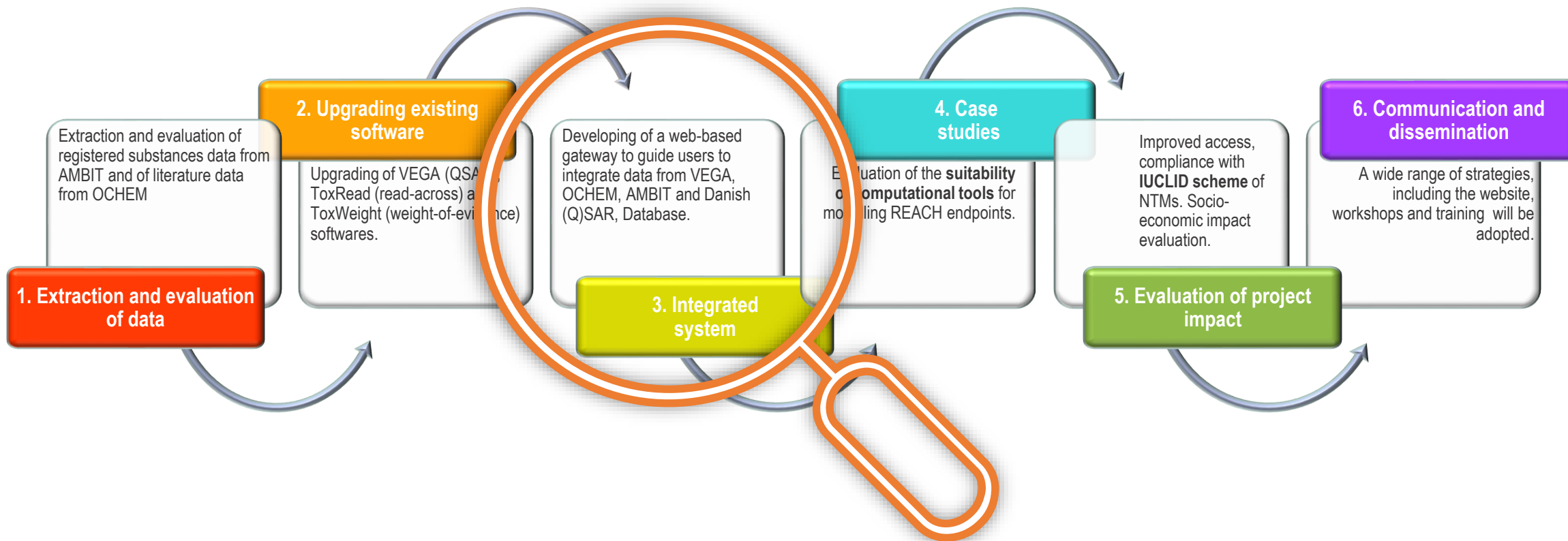


Evaluate the **potential impact** of CS in the  
EU by *exp + in silico*

**A big network** of systems offering non-  
testing methods (NTM) useful both for  
authorities and industries.



# PROJECT ACTIVITIES



# THE TOOLS



The network is composed of **VEGA**, the **Danish (Q)SAR Database**, **OCHEM** for the *in-silico models*, and for the read across workflow and data from the registered substances, of **ToxRead** and **AMBIT**.

# THE TOOLS



112 (Q)SAR freely available models for regulatory purposes.

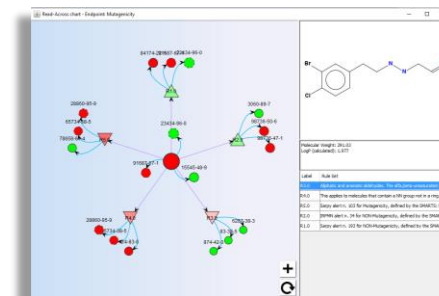
Different areas:

- Human toxicity
- Eco-toxicity
- Environmental
- Physico-chemical
- Toxicokinetics



Reproducible read-across evaluation for 23 endpoints showing similar compounds and SAs in common between chemicals.

**TOXREAD**



# THE TOOLS



**ECHA**  
EUROPEAN CHEMICALS AGENCY

**Ministry of Environment and Food of Denmark**  
Environmental Protection Agency

## Danish (Q)SAR Database

650,000 Substances

Enter Danish (Q)SAR Models

## DQ DATABASE

Estimates for **more than 650,000 substances** obtained with **more than 200 (Q)SARs** from free and commercial platforms.

## DQ MODELS

New portal to access some of the models of the database directly, also for new substances.

**Downloadable QPRF** report is generated.

# THE TOOLS



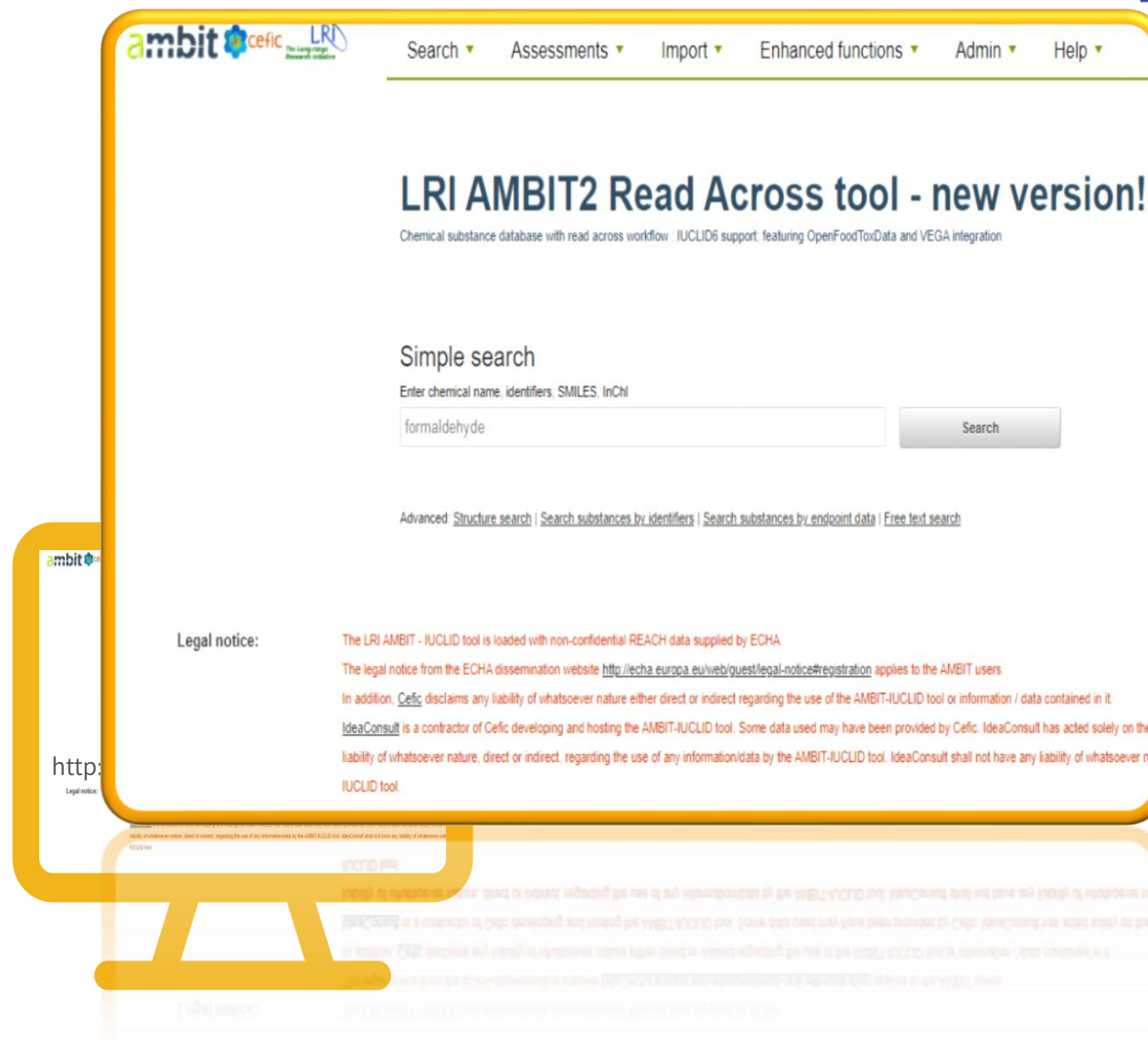
LIFE17 GIE/IT/000461

The OCHEM package offers a database of molecules and their ADMET properties.

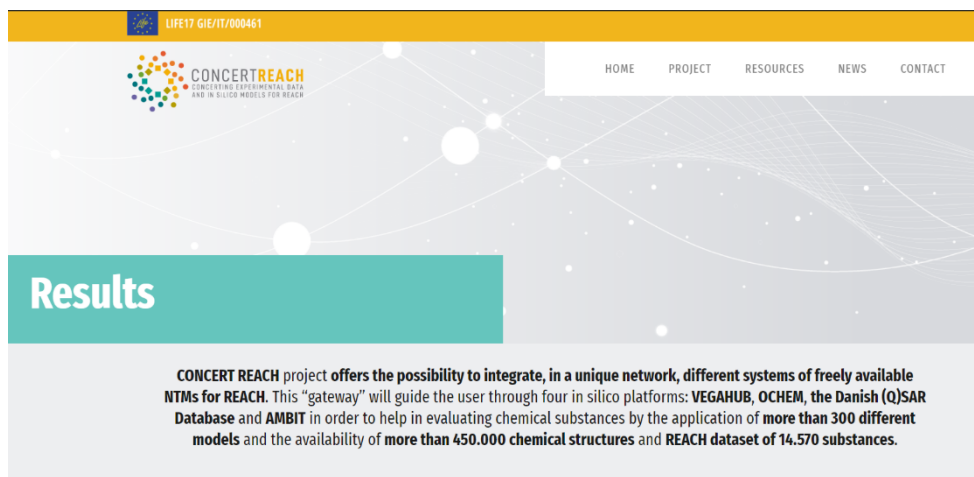
OCHEM contains more than **1 million** experimental records for about 499 properties collected from 12428 sources

# THE TOOLS

The AMBIT system consists of a database including more than **450.000 chemical** structures and REACH data on **14.570 substances**





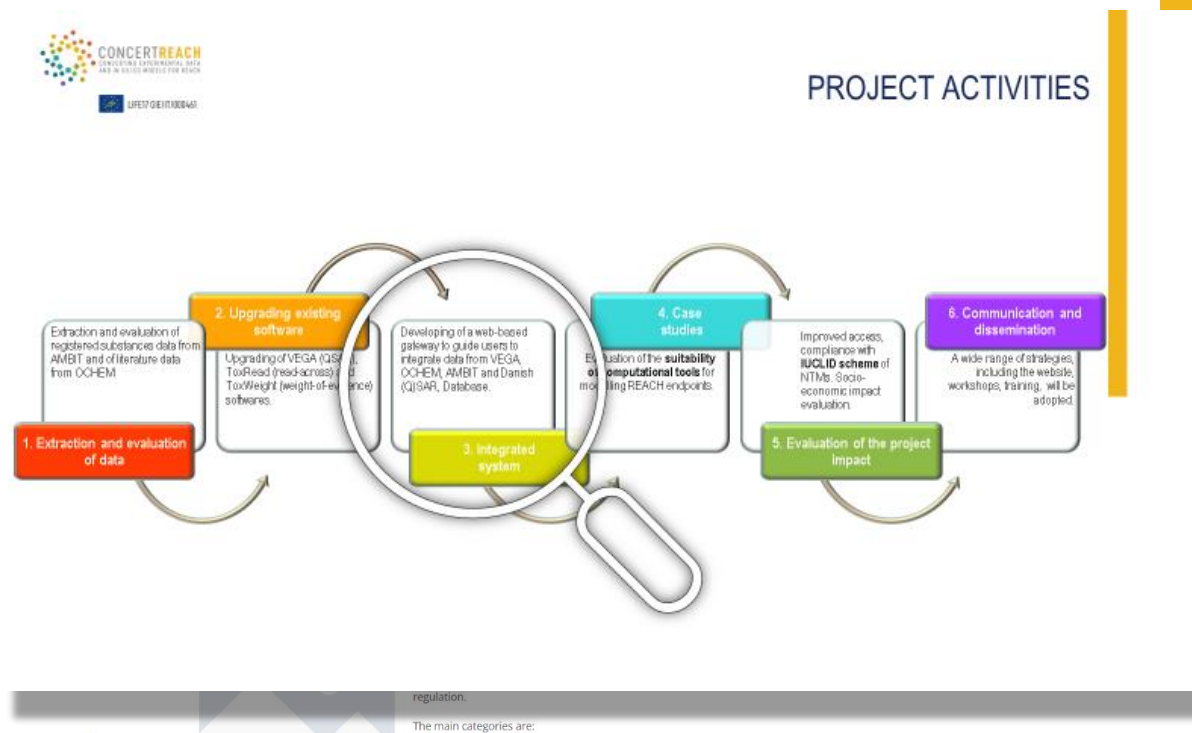


**Results**

**CONCERT REACH project offers the possibility to integrate, in a unique network, different systems of freely available NTMs for REACH. This "gateway" will guide the user through four in silico platforms: VEGA HUB, OCHEM, the Danish (Q)SAR Database and AMBIT in order to help in evaluating chemical substances by the application of more than 300 different models and the availability of more than 450.000 chemical structures and REACH dataset of 14.570 substances.**

The "gateway" reports all the predictive software available in the four platforms relative to REACH endpoints.

However, please consider that we cannot guarantee that they are correct and usable for the REACH legislation. Additionally, if industry wants to use the result from a certain model, it has to verify if this is legally legitimate. For certain very specific endpoints we have reported models that may have been developed using more general data. These models may not perfectly adhere to the endpoint.



<https://www.life-concertreach.eu/results/>



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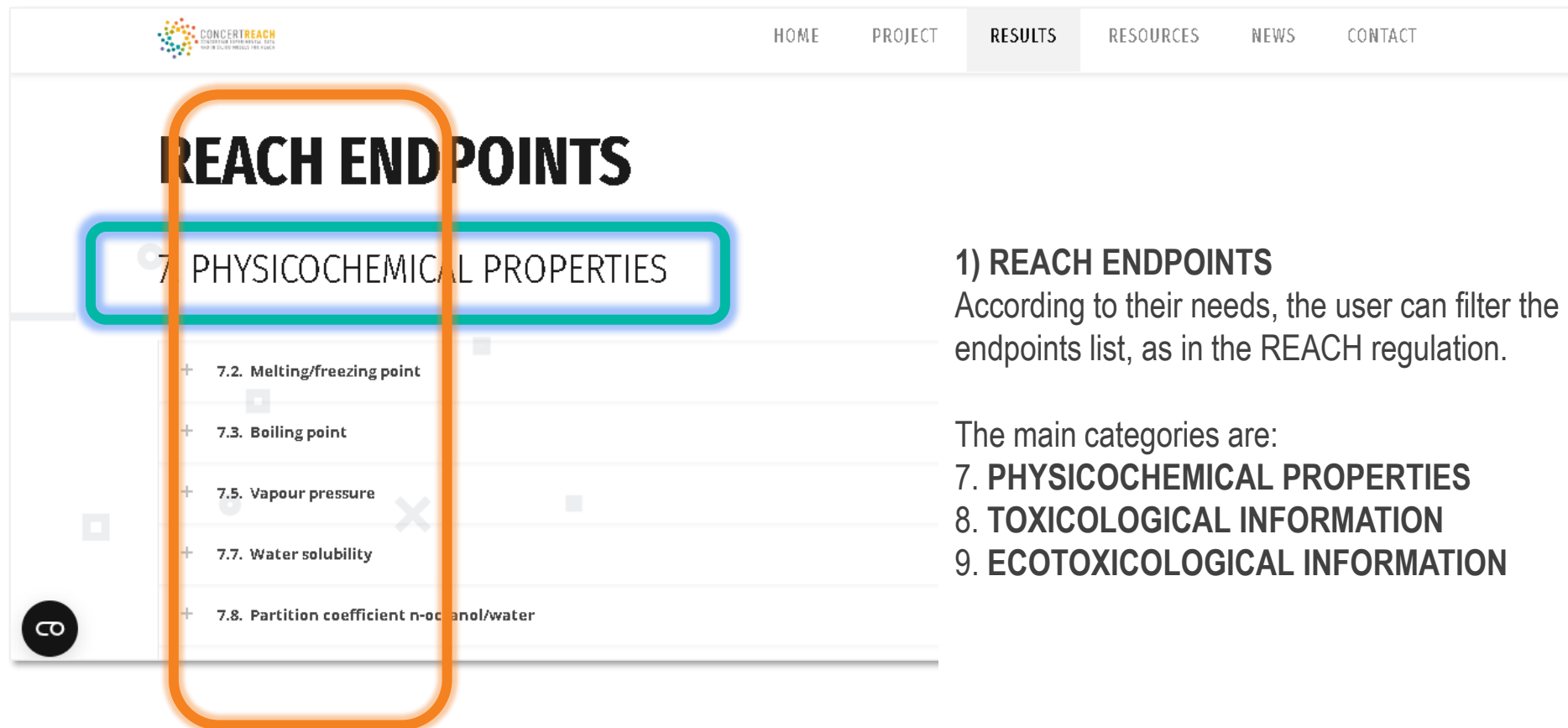
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WHIDE ENGAGEMENT  
OF  
**AUTHORITIES AND INDUSTRY**

<https://www.life-concertreach.eu/results/>



CONCERTREACH  
CONCERTING EXPERIMENTAL DATA  
AND IN SILICO MODELS FOR REACH

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## REACH ENDPOINTS

### 7. PHYSICOCHEMICAL PROPERTIES

- + 7.2. Melting/freezing point
- + 7.3. Boiling point
- + 7.5. Vapour pressure
- + 7.7. Water solubility
- + 7.8. Partition coefficient n-octanol/water

### 1) REACH ENDPOINTS

According to their needs, the user can filter the models by the endpoints list, as in the REACH regulation.

The main categories are:

- 7. PHYSICOCHEMICAL PROPERTIES
- 8. TOXICOLOGICAL INFORMATION
- 9. ECOTOXICOLOGICAL INFORMATION

### 2) SELECTION OF THE SUITABLE MODEL

<https://www.life-concertreach.eu/results/>



# REACH ENDPOINTS

## 7. PHYSICOCHEMICAL PROPERTIES

+ 7.2. Melting/freezing point

+ 7.3. Boiling point

+ 7.5. Vapour pressure

+ 7.7. Water solubility






+ 7.8. Partition coefficient n-octanol/water

+ 7.16. Dissociation constant

+ 7.5. Vapour pressure

- 7.7. Water solubility

All **VEGA AND ToxRead** DANISH QSAR DATABASE **AMBIT** OCHEM

| End Point                              | Model  | Type       | Dataset size | Training set size | Test set size | Platform           | Remarks  |
|--|--|------------|--------------|-------------------|---------------|--------------------|--|
| P-CHEM 4.8. Water solubility           | <a href="#">Dataset</a>                                      |            | 18126        |                   |               | AMBIT              |  |
| P-CHEM, 4.8 water solubility, OECD 105 | <a href="#">Water solubility model (IRFMN)</a>               | continuous | 5018         | 4014              | 1004          | VEGA               |   |
| P-CHEM, 4.8 water solubility, OECD 105 | <a href="#">Water solubility from Kow (mg/L) (EPI)</a>       | continuous |              |                   |               | DanishQSARDatabase |    |
| P-CHEM, 4.8 water solubility, OECD 105 | <a href="#">Water solubility from Fragments (mg/L) (EPI)</a> | continuous |              |                   |               | DanishQSARDatabase |   |
| Water solubility                       | <a href="#">ASNN</a>   | continuous |              | 1311              |               | OCHEM              | <br> |

### 3) PREDICTING

Once selected the model of interest, click on the link present in the “model” column; you will be redirected to the access page of the models.

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Once selected the model of interest, click on the link present in the “model” column; you will be redirected to the access page of the models.



## 4) INTERPRETATION OF THE RESULTS

The user can consult all the available documentation of the *in silico* tools in the dedicated section.



Environment International

Volume 131, October 2019, 105060



Review article

### Integrating *in silico* models and read-across methods for predicting toxicity of chemicals: A step-wise strategy

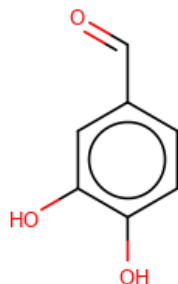
Emilio Benfenati <sup>a</sup>  , Qasim Chaudhry <sup>b</sup>, Giuseppina Gini <sup>c</sup>, Jean Lou Dorne <sup>d</sup>

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# Target molecule Tools Assessment



3,4-Dihydroxybenzaldehyde  
O=Cc1ccc(O)c(O)c1  
Genetic toxicity in vitro.  
Ames test



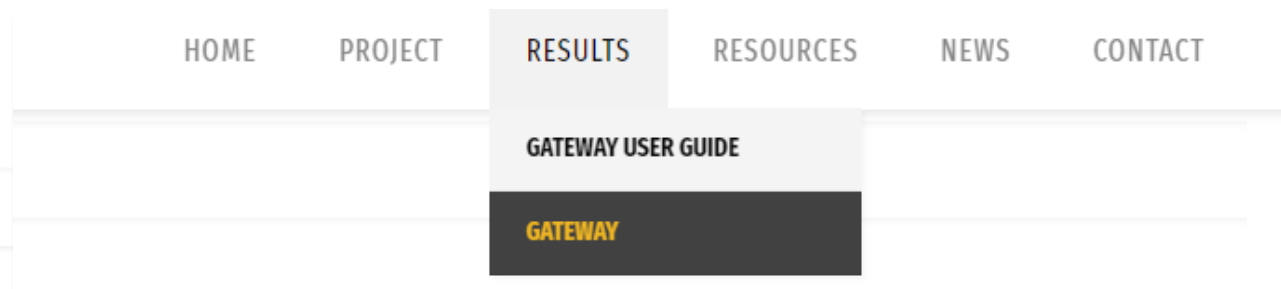
- Checking the availability of the tools for the endpoint in the gateway
- Running the models



OUTPUTS  
INTERPRETATION






# Checking the availability of the tools for in vitro gene mutation in bacteria in the CONCERT REACH gateway



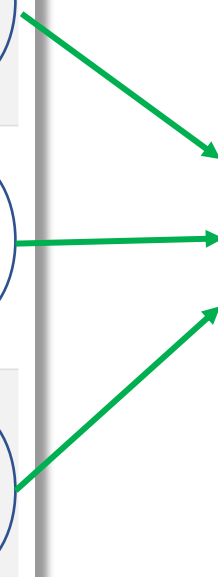
## 8.4.1. In vitro gene mutation study in bacteria

All VEGA AND ToxRead DANISH QSAR DATABASE AMBIT OCHEM

| End Point  | Model  | Type           | Dataset size | Training set size | Test set size | Cross-validation procedure | Platform | Remarks   |
|--|--|----------------|--------------|-------------------|---------------|----------------------------|----------|---|
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) CONSENSUS model         | classification | 0            | 0                 | 0             |                            | VEGA     |    |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (CAESAR)          | classification | 4204         | 3367              | 837           |                            | VEGA     |   |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (KNN-Read-Across) | classification | 5770         | 5770              | 0             |                            | VEGA     |  |

Currently **23 Models** from **VEGA**, **Danish (Q)SAR Database** and **OCHEM**  
 (Statistical&knowledge-based)  
**1** module of **ToxRead**  
 (read-across)  
**1** dataset of **AMBIT**

**Direct link to the documentation:**  
 QMRF, papers or guides



# Checking the availability of the tools for in vitro gene mutation in bacteria in the CONCERT REACH gateway

8.4.1. In vitro gene mutation study in bacteria

ALL VEGA AND ToxRead DANISH QSAR DATABASE AMBIT OCHEM

| End Point  | Model  | Type                     | Dataset size | Training set size | Test set size | Cross-validation procedure | Platform | Remarks |
|--|--|--------------------------|--------------|-------------------|---------------|----------------------------|----------|---------|
| TOX 7.6.1. Genetic toxicity in vitro                       | Mutagenicity   | reproducible read-across | 6060         |                   |               |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) CONSENSUS model                     | classification           | 0            | 0                 | 0             |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (CAESAR)                      | classification           | 4204         | 3367              | 837           |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (KNN-Read-Across)             | classification           | 5770         | 5770              | 0             |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (ISS)                         | classification           | 670          | 670               | 0             |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (SarPy-IRFMN) (version 1.0.8) | classification           | 4204         | 3367              | 837           |                            | VEGA     |         |

## VEGA

4 individual models + 1 consensus

- CAESAR - **Hybrid** model (statistical + knowledge-based)
- KNN-Read-Across - **read-across** model
- ISS - **knowledge-based** structural alerts (Benigni-Bossa rule-base)
- SarPy-IRFMN - **statistical** structural alerts

# Checking the availability of the tools for in vitro gene mutation in bacteria in the CONCERT REACH gateway

## 8.4.1. In vitro gene mutation study in bacteria

ALL **VEGA AND ToxRead** DANISH QSAR DATABASE AMBIT OCHEM

| End Point  | Model  | Type                     | Dataset size | Training set size | Test set size | Cross-validation procedure | Platform | Remarks |
|--|--|--------------------------|--------------|-------------------|---------------|----------------------------|----------|---------|
| TOX 7.6.1. Genetic toxicity in vitro                       | Mutagenicity   | reproducible read-across | 6060         |                   |               |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) CONSENSUS model                     | classification           | 0            | 0                 | 0             |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (CAESAR)                      | classification           | 4204         | 3367              | 837           |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (KNN-Read-Across)             | classification           | 5770         | 5770              | 0             |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (ISS)                         | classification           | 670          | 670               | 0             |                            | VEGA     |         |
| TOX 7.6.1. Genetic toxicity in vitro. Ames test (OECD 471) | Mutagenicity (Ames test) model (SarPy-IRFMN) (version 1.0.8) | classification           | 4204         | 3367              | 837           |                            | VEGA     |         |

## ToxRead - 1 module

Dataset = 6060 substances and their public data

4 different rulesets:

- ISS (**knowledge-based structural alerts**)
- SARpy (**statistical structural alerts**)
- CSR4 (**statistical structural alerts**)
- IRFMN (**knowledge-based structural alerts**)

# Checking the availability of the tools for in vitro gene mutation in bacteria in the CONCERT REACH gateway

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8.4.1. In vitro gene mutation study in bacteria

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ALL VEGA AND ToxRead DANISH QSAR DATABASE AMBIT OCHEM

| End Point            | Model  | Type           | Dataset size | Training set size | Test set size | Cross-validation procedure              | Platform             | Remarks |
|----------------------|--|----------------|--------------|-------------------|---------------|---|----------------------|---------|
| Ames test (OECD 471) | Bacterial reverse mutation test (Ames test in <i>S. typhimurium</i> in vitro) (CASE Ultra) | classification |              | 4102              |               | 5 times 2-fold external crossvalidation | Danish QSAR Database |         |
| Ames test (OECD 471) | Bacterial reverse mutation test (Ames test in <i>S. typhimurium</i> in vitro) (Leadscope)  | classification |              | 4102              |               | 5 times 2-fold external crossvalidation | Danish QSAR Database |         |
| Ames test (OECD 471) | Bacterial reverse mutation test (Ames test in <i>S. typhimurium</i> in vitro) (SciQSAR)    | classification |              | 4102              |               | 5 times 2-fold external crossvalidation | Danish QSAR Database |         |
| Ames test (OECD 471) | Direct acting Ames mutagens (without S9) - ONLY use for Ames POS_IN (CASE Ultra)           | classification |              | 388               |               | 5 times 2-fold external crossvalidation | Danish QSAR Database |         |
| Ames test (OECD 471) | Direct acting Ames mutagens (without S9) - ONLY use for Ames POS_IN (Leadscope)            | classification |              | 388               |               | 5 times 2-fold external crossvalidation | Danish QSAR Database |         |
| Ames test (OECD 471) | Direct acting Ames mutagens (without S9) - ONLY use for Ames POS_IN (SciQSAR)              | classification |              | 388               |               | 5 times 2-fold external crossvalidation | Danish QSAR Database |         |
| Ames test            | Base pair Ames mutagens -  |                |              |                   |               | 5 times 2-fold                          |                      |         |

## Danish (Q)SAR Database

15 statistical models and 2 knowledge-based alert profilers

- Bacterial reverse mutation test (Ames test in *S. typhimurium* in vitro)
- Direct acting Ames mutagens (without S9)
- Base pair Ames mutagens
- Frame shift Ames mutagens
- Potent Ames mutagens, reversions  $\geq 10$  times controls

## Profilers (OECD QSAR Toolbox V.4.2)

- DNA alerts for AMES by OASIS, alerts in parent only
- In vitro mutagenicity (Ames test) alerts by ISS, alerts in parent only

# Checking the availability of the tools for in vitro gene mutation in bacteria in the CONCERT REACH gateway


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**GATEWAY**

## 8.4.1. In vitro gene mutation study in bacteria

ALL VEGA AND ToxRead DANISH QSAR DATABASE AMBIT **OCHEM**

| End Point            | Model | Type           | Dataset size | Training set size | Test set size | Cross-validation procedure | Platform | Remarks   |
|----------------------|-------|----------------|--------------|-------------------|---------------|----------------------------|----------|---|
| Ames test (OECD 471) | ASNN  | Classification |              | 4361              | 2181          |                            | OCHEM    |  |

**OCHEM**  
1 statistical model & ToxAlert match

ALL VEGA AND ToxRead DANISH QSAR DATABASE **AMBIT** OCHEM

| End Point                            | Model   | Type | Dataset size | Training set size | Test set size | Cross-validation procedure | Platform | Remarks   |
|--------------------------------------|---------|------|--------------|-------------------|---------------|----------------------------|----------|---|
| TOX 7.6.1. Genetic toxicity in vitro | Dataset |      | 50366        |                   |               |                            | AMBIT    |  |

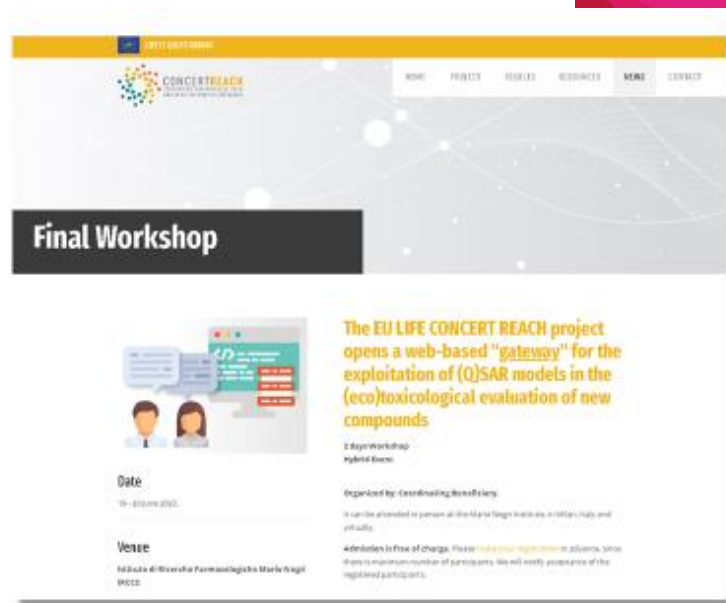
**AMBIT**  
1 dataset

## Tuesday 20/06, morning Training sessions

2-day workshop

Monday 19/06, full day  
Workshop presentations

Tuesday 20/06, morning  
Training sessions



The screenshot shows the CONCERT REACH website with a navigation menu (HOME, PROJECTS, RESULTS, RESOURCES, NEWS, CONTACT) and a main heading 'Final Workshop'. Below the heading is a graphic with two people and a computer screen. The text reads: 'The EU LIFE CONCERT REACH project opens a web-based "gateway" for the exploitation of (Q)SAR models in the (eco)toxicological evaluation of new compounds'. It specifies a '2 days workshop - hybrid event' on '19 - 20 June 2020' at the 'Venue: Istituto di Ricerche Farmacologiche Mario Negri IMCC'. It is organized by 'Coordinating Beneficiary' and is 'Admission is free of charge. There is a maximum number of participants. We will verify the presence of the registered participants.'

# THANKS

Does anyone have any questions?  
<https://www.life-concertreach.eu/>



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