CONCERTREACH
CONCERTING EXPERIMENTAL DATA AND IN SILICO MODELS FOR REACH

LIFE17 GIE/IT/000461

Life Concert REACH project

Emilio Benfenati,

Istituto di Ricerche Farmacologiche Mario Negri

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THE PROJECT

plans to establish a

big network of systems

offering non-testing methods

(NTM) useful both for

authorities and industries..

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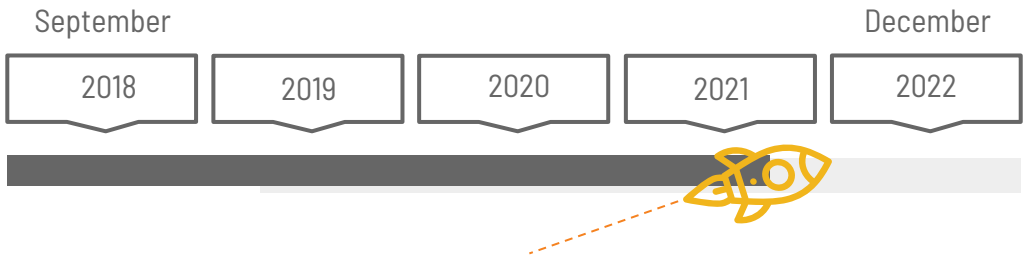
THE PROJECT



ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS

Istituto di Ricerche Farmacologiche Mario Negri, Italy
Research institute, **Coordinator**

Associated Beneficiaries

big chem
DTU
knoell worldwide registration
kode from data to knowledge
Sviluppo chimica spa

IOEA Consult

External supporting

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THE PROJECT

01

Policy landscape .

EU chemicals regulation, the so-called **REACH** regulation.

02

Non-testing methods - NTMs

The regulation raises the need to use **alternative methods** to protect environmental and human health, including the application of innovative **non-testing methods (NTMs),** and to determine the impact of substances with reliable environmental indicators.

03

REACH experimental data

Since May 2018, a huge amount of REACH experimental data has become available, which now needs to be better exploited, especially through NTMs.

04

Integrated network of systems

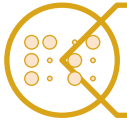
VEGA, the Danish (Q)SAR Database, OCHEM and AMBIT are the main components of this new network offering an improved version of these tools for the in silico and read-across evaluation of chemicals.

OBJECTIVES

To boost the data of registered chemicals improving in silico tools and read-across, offering **more than 300 in silico models**.

To make available **42 new in silico models**.

To make available a **new tool for grouping**



To extensively implement **read-across tools**, freely available and user-friendly

To integrate the results of read-across and *in silico* models (**weight-of-evidence**).

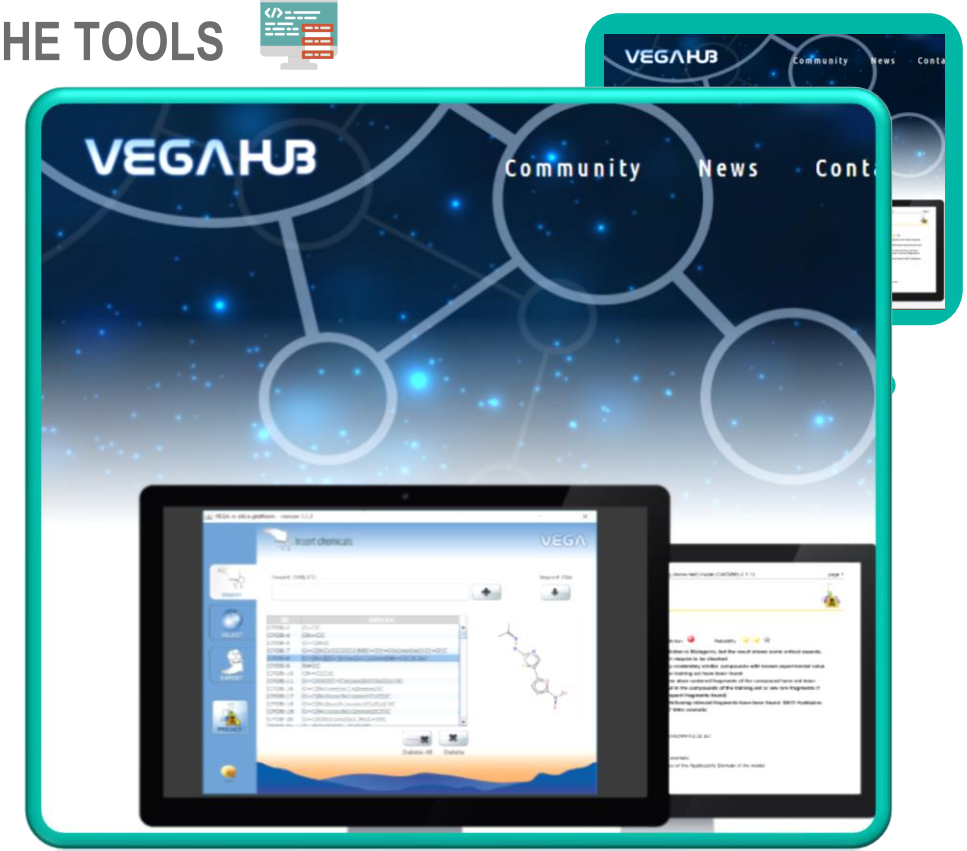
To facilitate the work assessors of substances of REACH

To evaluate **the impact of REACH** through an integration of experimental data of registered substances and in silico tools.

THE TOOLS

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

THE TOOLS



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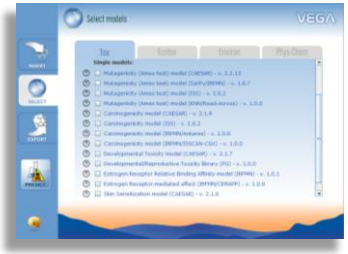
80 (Q)SAR freely available models for regulatory purposes.

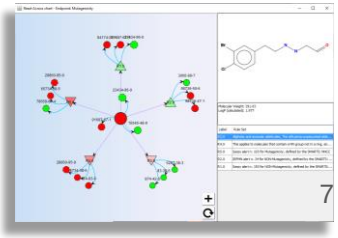
VEGA

Different areas:
-Human toxicity
-Eco-toxicity
-Environmental
-Physico-chemical
-Toxicokinetics



Reproducible **read-across evaluation** for 20 endpoints showing **similar compounds** and **SAs** in common between chemicals.

TOXREAD



THE TOOLS

DQ DATABASE

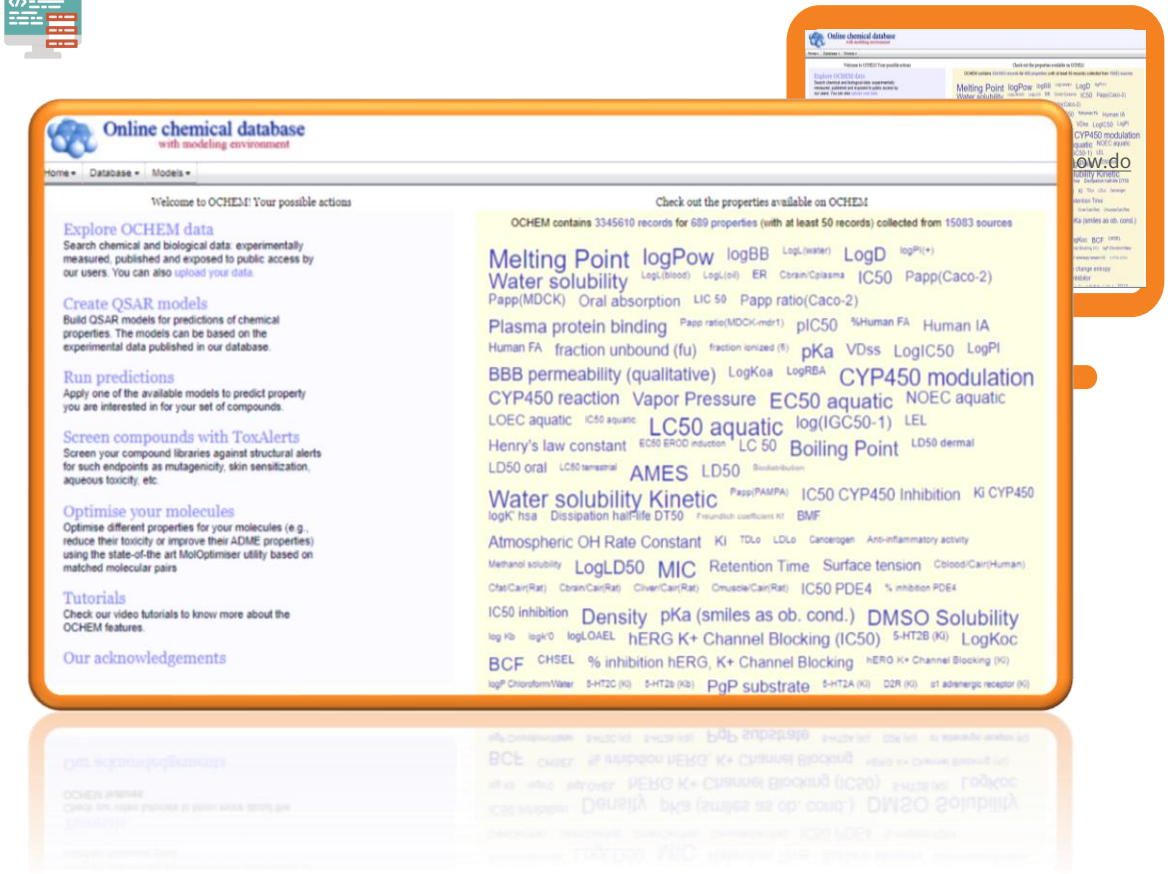
Estimates for **more than 650,000 substances** obtained with **more than 200 (Q)SARs** from free and commercial platforms.

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

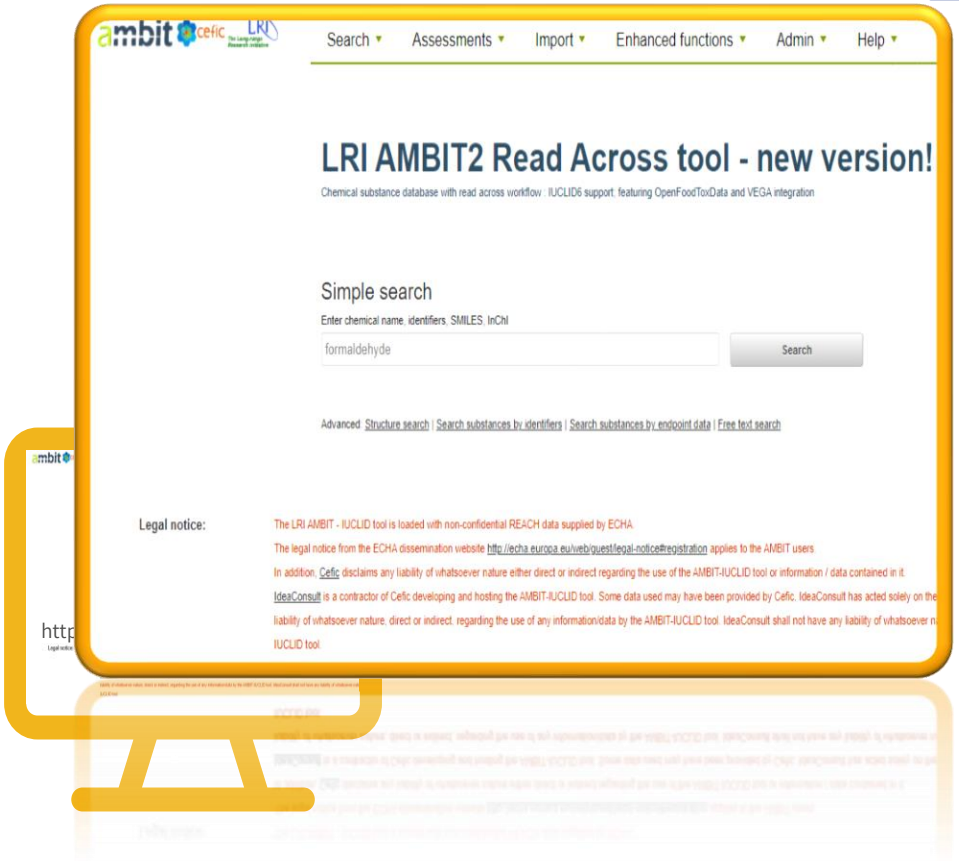


The OCHEM package offers a **database of molecules** and their **ADMET properties.**

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**



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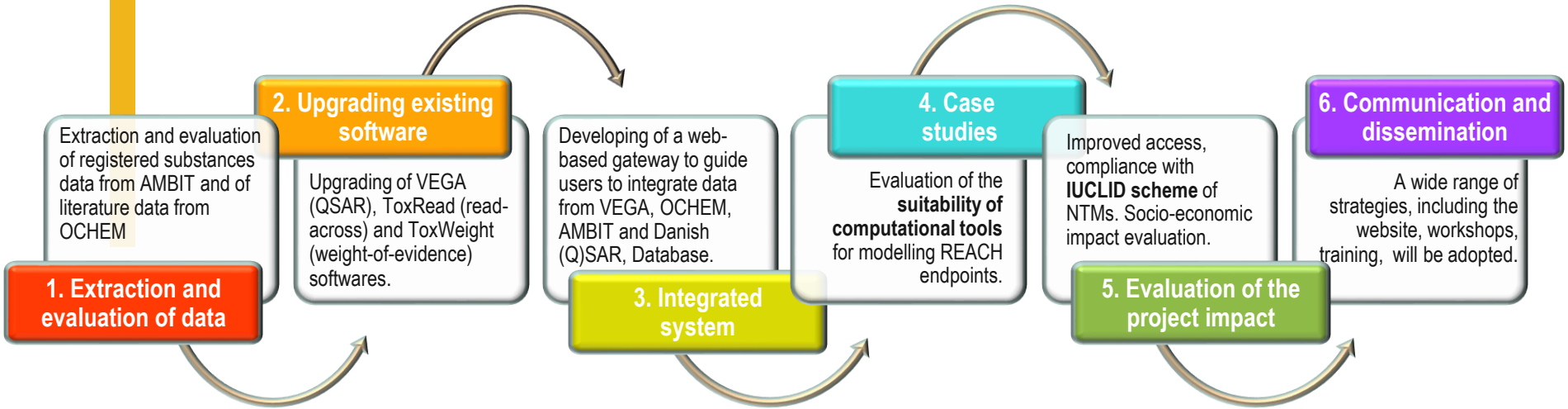
PROJECT ACTIVITIES



SOME RESULTS

- Protocol to access data from ECHA
- 18 models implemented in VEGA, based on existing models
- Development of more than 40 new models for selected REACH endpoints
- Grouping – optimization of procedure on a pilot endpoint
- Rules for read across
- Impact of REACH on the production and importation of chemicals in Italy from 2015 to 2020

SOME RESULTS

Protocol to access data from ECHA

AMBIT

- **Experimental data pruning** (keeping): exp result, key study, Klimisch 1&2 and only guidance reported.
- **Modelling purpose pruning** (keeping): monocostituents; organic compounds; values not as ranges; salts/tautomers management
- **Endpoint specific pruning** (keeping): according to guidelines/methods requirements.

EChemPortal

- Simplify and collapse conclusions from experiments in few labels (e.g. corrosive, irritant, not irritant) with support by KNOELL
- Apply a **KNIME workflow** to retrieve SMILES string and structure cleaning for inorganics, organometallics and salts
- **Verify consistency** in experimental label assigned to each maintained structure

SOME RESULTS

18 models implemented in VEGA, based on existing models

TOX
NOAEL model
Carcinogenicity oral classification model
Carcinogenicity oral Slope Factor model
Carcinogenicity inhalation classification model
Carcinogenicity inhalation Slope Factor model
Skin Sensitization model
Androgen Receptor-mediated effect
Aromatase activity model
Chromosomal aberration model
In vitro Micronucleus activity model
In vivo Micronucleus activity model

ECOTOX
Daphnia Magna Acute (EC50) Toxicity model
Daphnia Magna Chronic (NOEC) Toxicity model
Algae Acute (EC50) Toxicity model
Algae Chronic (NOEC) Toxicity model
Fish Acute (LC50) Toxicity model

ENVIRON
Persistence (sediment) quantitative model
BCF model (Arnot-Gobas)

SOME RESULTS

Development of more than 40 new models for selected REACH endpoints

REACH endpoints

Selection

Eye irritation,
Melting point
Skin irritation
Skin sensitization
Terrestrial toxicity
Vapour pressure

Collection

Public sources

Development

SARpy, QSARpy,
CORAL, KNIME, R…

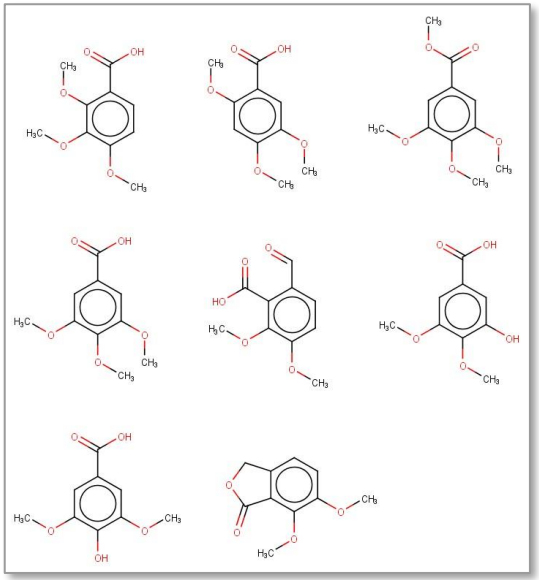
Validation

Selection

12 best models to be implemented In VEGA

SOME RESULTS

* Cluster no. 1-4 (average similarity: 0.939)



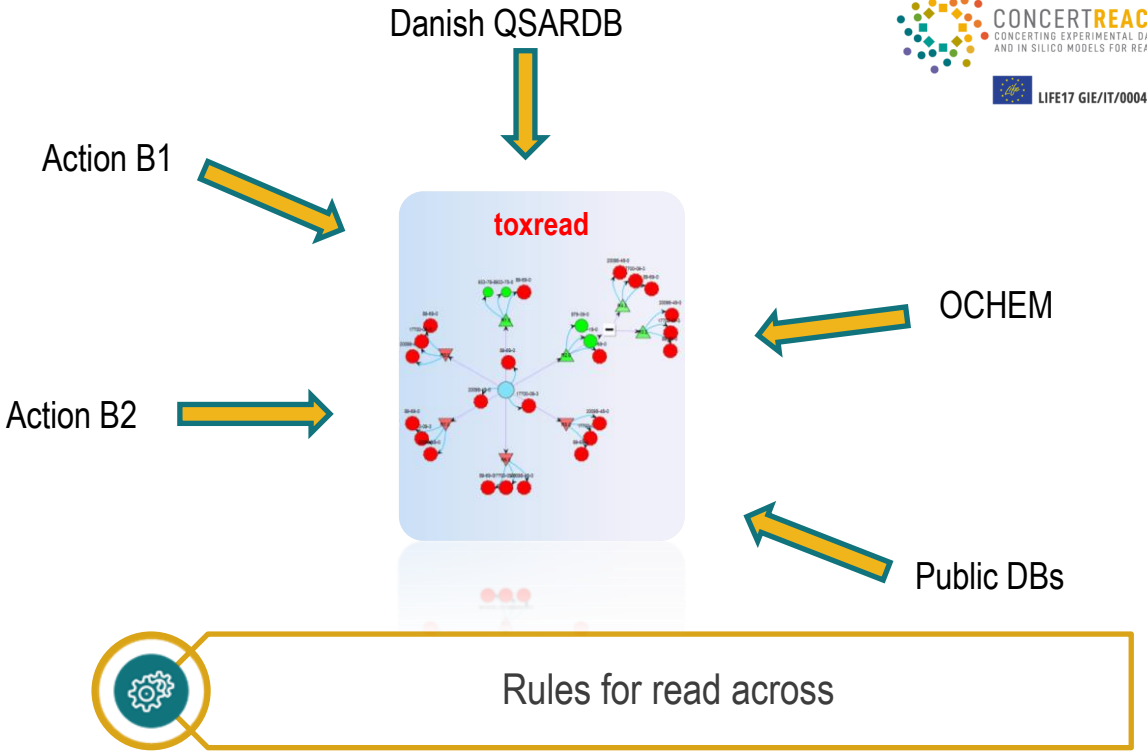
Grouping – otpimization of procedure on a pilot endpoint

- Exercise on the first case study – 3004 **melting point data**
- Definition of number of clusters - **154 super-clusters**

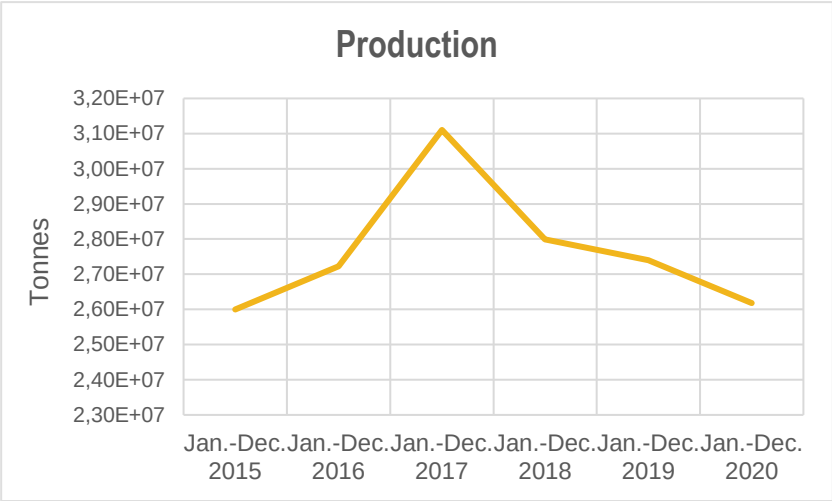
  e.g.Super-cluster no. 1 has 16 clusters.

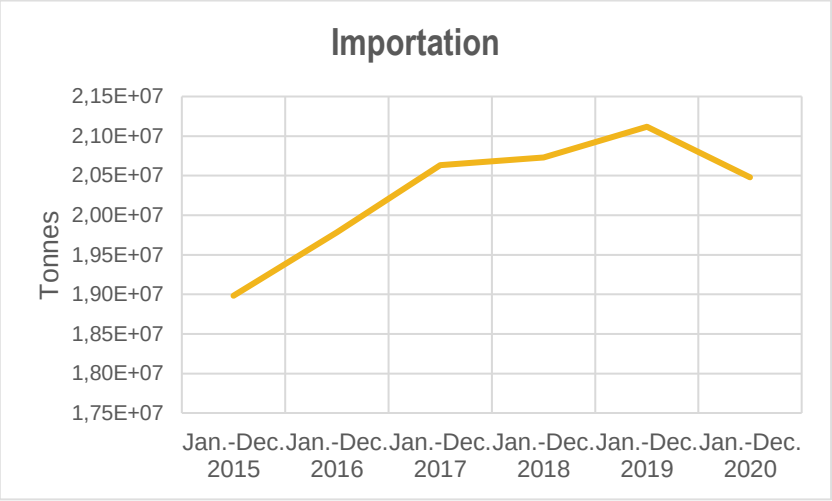
  Their average similaity ranges from 0.76 to 0.946
- Tuning of the tools

SOME RESULTS:
New sets of rules from



SOME RESULTS





Industrial gas, dyes and pigments, fertilizers and nitrogen compounds, pesticides, plastic materials, detergents, cosmetics ….

Impact of REACH on the production and importation of chemicals in Italy from 2015 to 2020

ONGOING

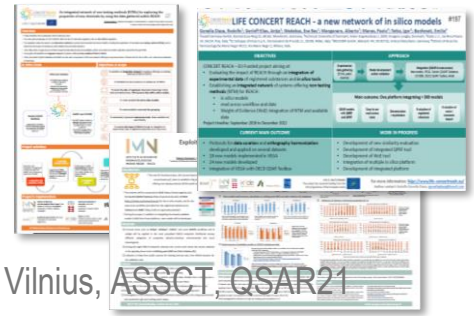
- Implementation in VEGA of the new models
- Read across – new concept of similarity
- New outcome of the models
- Integrating NTM
- Networking between platforms

Web site

https://www.life-concertreach.eu/

Notice Board

Posters presentations



Vilnius, ASSCT, QSAR21

LIFE logo – new layout, brochure..

THANKS

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

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