CONCERT REACH

CONCERTREACH
CONCERTING EXPERIMENTAL DATA AND IN SILICO MODELS FOR REACH

LIFE17 GIE/IT/000461

September **June**

2018 | 2019 | 2020 | 2021 | 2022 | 2023

Layman's report

LAYMAN'S REPORT CONTENT

CONCERTREACH
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ASSOCIATED BENEFICIARIES

Istituto di Ricerche Farmacologiche Mario Negri, Italy
Research Institute, project's coordinator, Developer of VEGA, ToxRead, VERA and SWAN

BIGCHEM GMbH, Germany
Develops and markets innovative IT solutions for the prediction of important properties of chemicals and drugs

Technical University of Danmark, Denmark
Developer of Danish (Q)SAR Database.

knoell Germany GmbH, Germany
Consultant for chemical's registration.

Kode s.r.l., Italy
Private company active in data science (chemometrics and chemoinformatics).

SC Sviluppo chimica S.p.A., Italy
Service company, part of the Italian Federation of the Chemical Industry.

OVERVIEW

The main policy landscape of LIFE CONCERT REACH is the EU chemicals regulation, the so-called **REACH regulation**, which in practice compels the industry to assess the safety of the chemicals it produces or imports. The regulation poses several challenges, which the project seeks to address. In particular, 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. At the same time, since May 2018 (the deadline for the registration of substances under the REACH regulation), a huge amount of REACH experimental data has become available, which now needs to be better exploited, especially through NTMs.

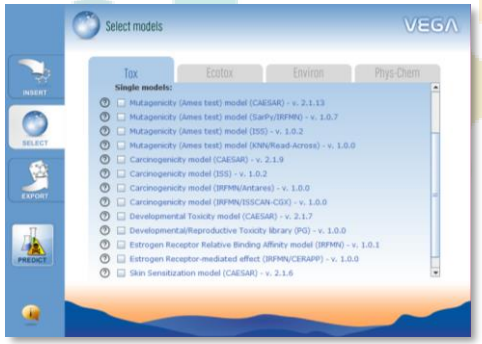
OVERVIEW

The project established an **integrated network** of systems offering freely available NTMs for REACH. The network combines tools widely used and supported by authorities and industry

VEGA together with **ToxRead** software, 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.

Quantitative Structure-Activity Relationship (**QSAR**) models and **read-across/grouping** strategies can be used to support the regulatory assessment of chemicals.

TOOLS' PROJECT - QSAR MODELS

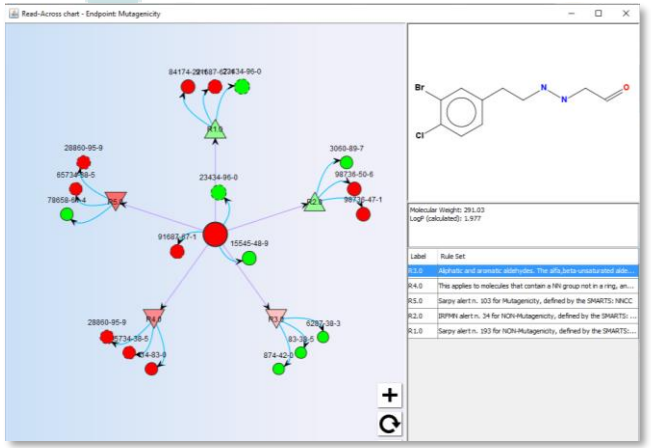


Using the **VEGA** platform, you can access a series of QSAR models for regulatory purposes. **112 of freely available (Q)SAR models** can be used to predict tox, ecotox, environ, and phys-chem properties of chemical compounds, using information obtained from chemical structures.

The **Danish (Q)SAR Database** includes estimates from more than **200 (Q)SARs** from **free and commercial** platforms and related to physicochemical properties, ecotoxicity, environmental fate, ADME and toxicity. (Q)SAR predictions for more than 600,000 chemical substances can be searched, sorting can be made on chemical similarity, and profiles of individual substances can be downloaded**.**

Within **OCHEM** platform it is possible to use more than 200 QSAR models, it is also possible to develop your own model. OCHEM contains more than **1 million** experimental records for about 5 hundred properties collected from several sources

TOOLS' PROJECT - READ-ACROSS APPROACH

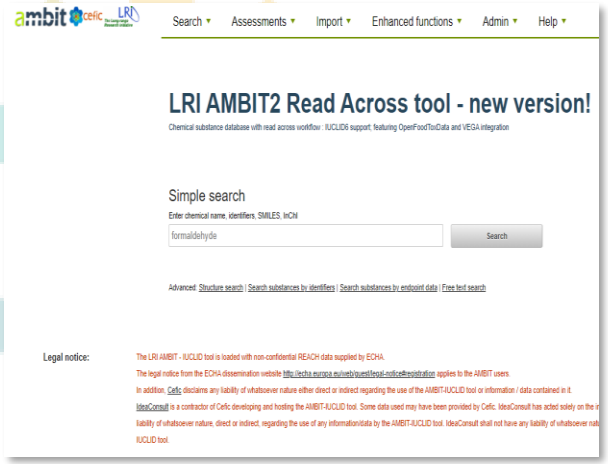


ToxRead performs reproducible **read-across evaluation** for **23 endpoints** showing similar compounds, structural alerts and relevant features in common among chemicals.

VEGA and ToxRead (both within VEGAHUB) have been used by **EFSA** to show examples of how to integrate the results of NTMs in a **weight-of-evidence strategy**.

The AMBIT system consists of a database including more than four hundred fifty thousand (**450.000) chemical** structures and REACH data on about fifteen thousand (**14.570) substances.** Users can search and access a wide range of existing information and predictions about a chemical.

Several in silico prediction models (e.g. **Toxtree**) are integrated in AMBIT. Molecular descriptors and structure alerts can be generated with this tool.



THE BIG NETWORK OF NON-TESTING METHODS (NTMS)

1. Supports the European Chemicals Agency (**ECHA**) in improving the use of NTMs

2. Offers **more than 450** freely available **in silico tools** within a single network

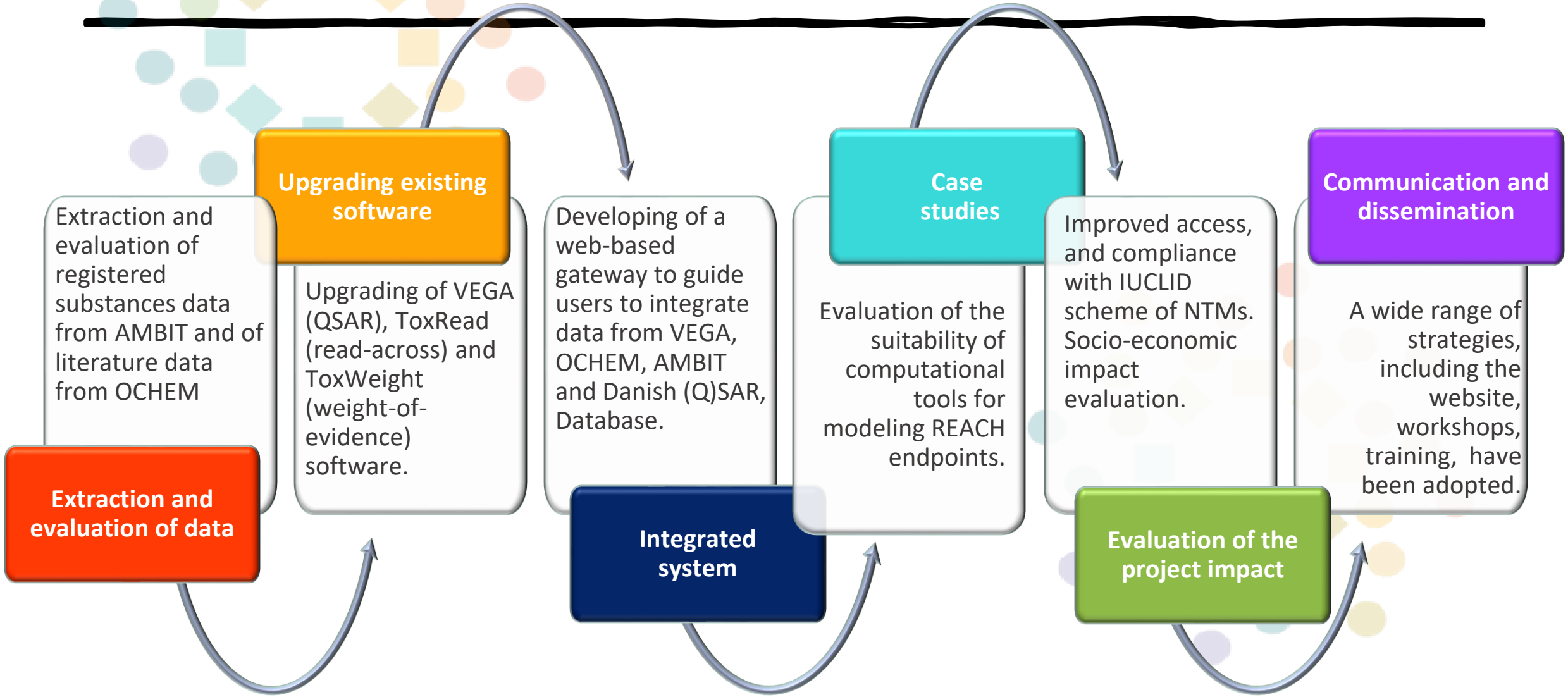
3. Makes **commercial in silico models freely available**, as well as read-across based on registered substances

4. Produces **new QMRFs** to facilitate the use of QSARs

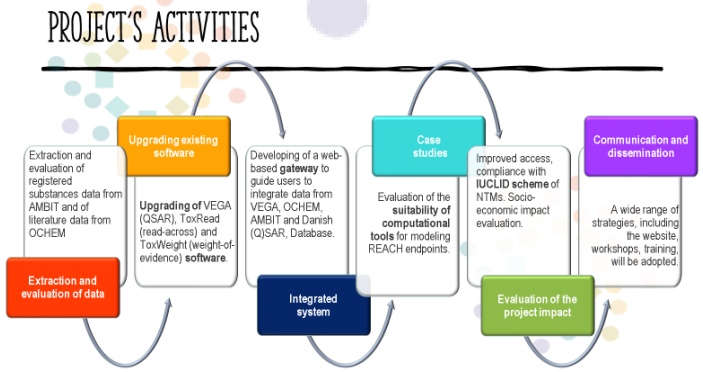
5. Prepared a **protocol** for the improved use of NTMs, as well as a protocol on how to manage conflicting values from different NTMs

6. Showed the practical use of NTMs, thanks to **a series of case studies**

PROJECT'S ACTIVITIES



FROM THE ACTIVITIES TO THE RESULTS



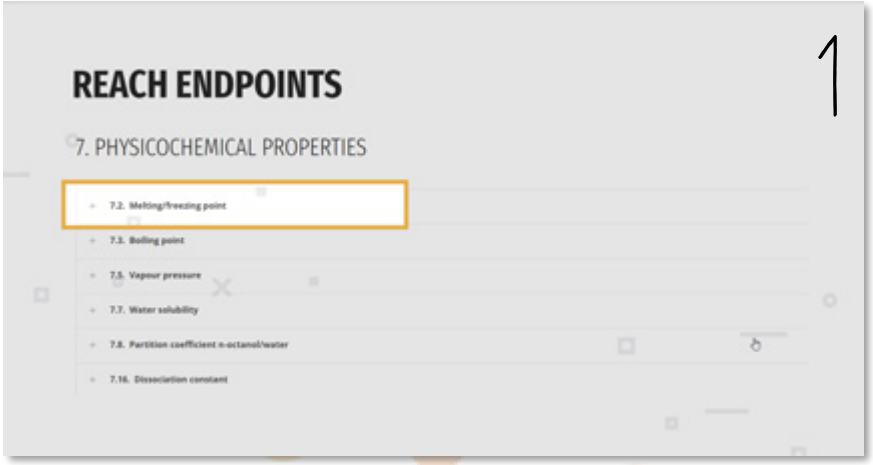
- **42 new in silico models** implemented in the updated version of VEGA platform
- A new tool for grouping, implementing a new concept of similarity new **VERA software**
- **Updated version of read-across** tools, freely available and user-friendly
- New strategy integrating the results of read-across and in silico models (weight-of-evidence), **new SWAN software**.
- The web-based **gateway**
- **Revision of the models' documentation** (QMRFs, output of the predictions, QPRFs)
- Extensively dissemination activity
- Strong **network with industry and regulators**

THE WEB-BASED GATEWAY

THE "GATEWAY" REPORTS ALL THE PREDICTIVE SOFTWARE AVAILABLE IN THE FOUR PLATFORMS RELATIVE TO REACH ENDPOINTS.

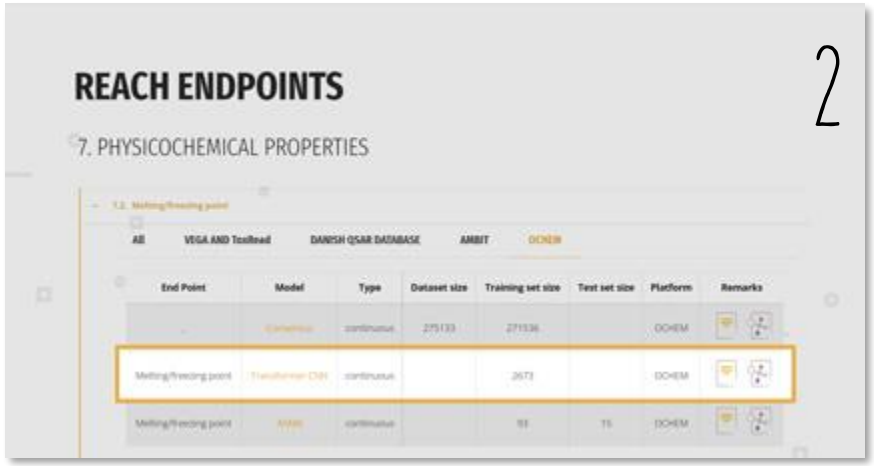
1) REACH ENDPOINTS

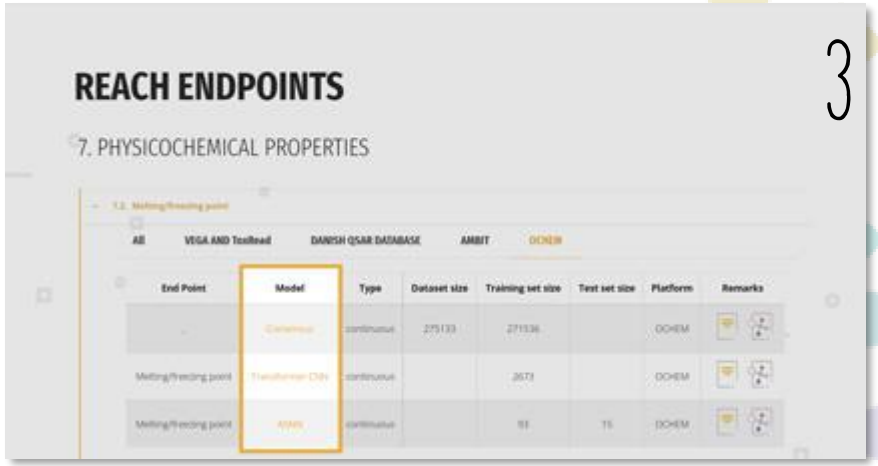
According to his/her needs, the user can filter the models by the endpoints list, as in the REACH regulation. The main categories are: 7. Physico-chemical properties, 8&9 (Eco)toxicological information. In addition to the REACH's categories, the gateway reports the models also for ENDOCRINE



2) SELECTION OF THE SUITABLE MODEL

For each endpoint, the gateway reports a list of the available models with their basilar information: name and classification f the model, size of the datasets and model's documentation like QMRF and papers..

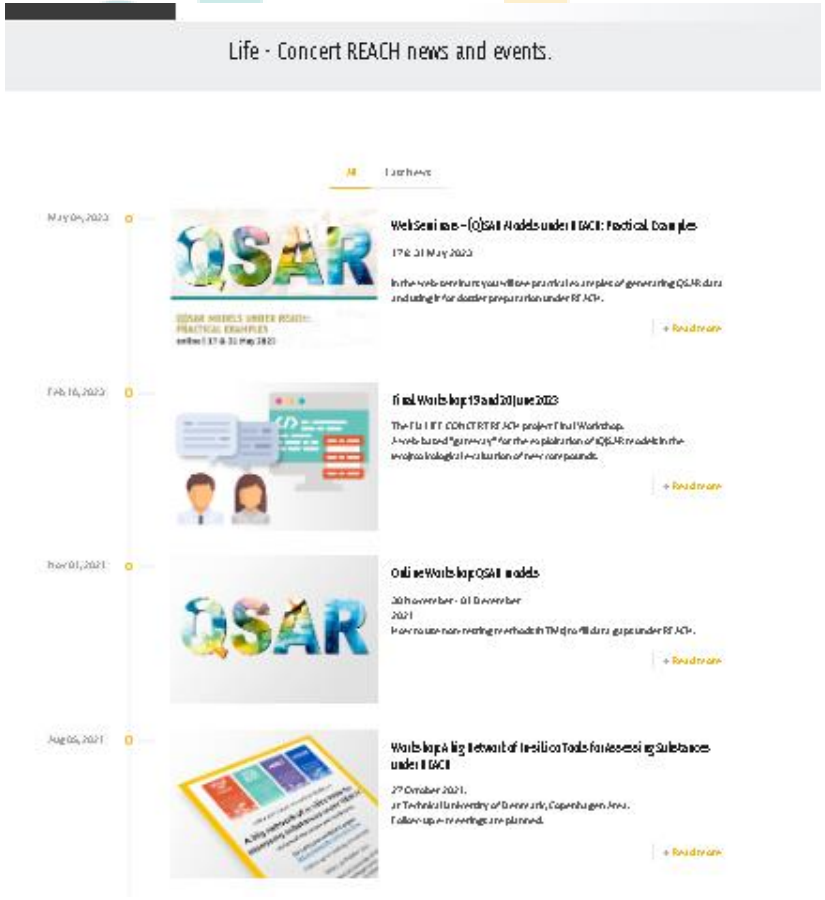




3) PREDICTING

Once selected the model of interest, click on the link present in the "platform" column; you will be redirected to the access page of the models. Each platform works differently:

DISSEMINATION & TRANSFERABILITY



7 workshops have been organized during the project. Most of them were organized virtually due to the pandemic situation.

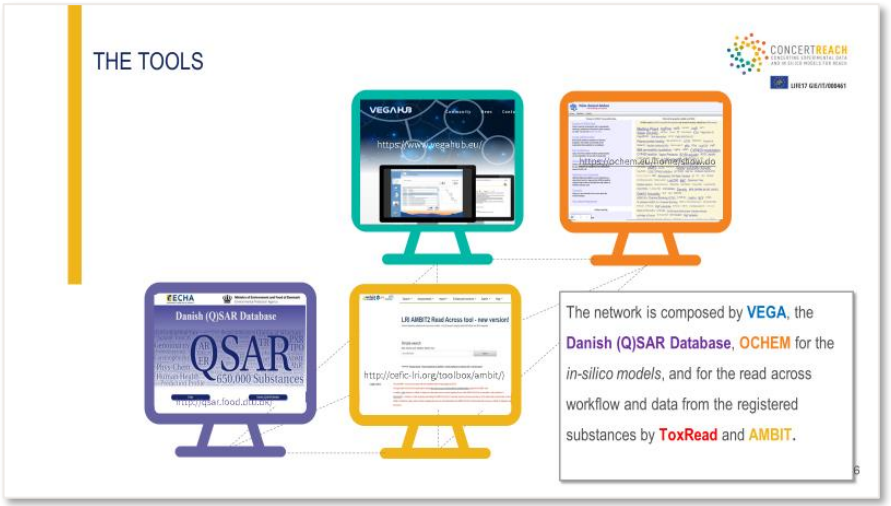
- **2** for **industrial stakeholders**, in Italy and Germany.
- **1** for **authorities**, inviting representatives of Member States, ECHA, EFSA, EEA, and JRC.
- **3** for **cosmetics, pesticides, and food ingredients and contaminants**, for networking purposes.
- **1 final workshop** (more than 100 participants). It was a 2-day hybrid event (both online and in person, at the Mario Negri Institute, in Milan). During the final workshop, representatives of industries and their associations, authorities such as ECHA and EFSA, and academics have participated. Representatives of NGO have been invited too

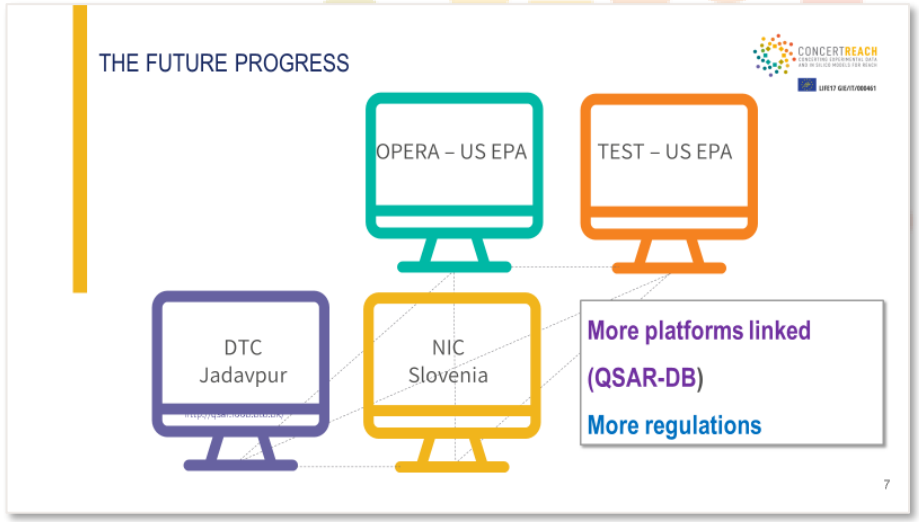
2 web seminars for industry, online events with more than 100 participants. related to the release of the gateway and its promotion, as well as the presentation of the case studies and the new VERA tool for automated read-across.

DISSEMINATION & TRANSFERABILITY

- The **web portal** of the project is online at the link https://www.life-concertreach.eu/.
- Thanks to the project**, 54** scientific papers have been written.
- **Training activities** involving internships for students and specific courses on VEGAHUB, OCHEM, AMBIT and Danish (Q)SAR database.
- **Platforms linked**: predictions from 18 VEGA models have been generated and included in the Danish (Q)SAR Database.

- It is planned to transfer the gateway concept to different on top of REACH (Foods, Cosmetics, Pesticides, Biocides, Pharma, Contaminants) and extend the number of the platforms involved .





IMPACTS' PROJECT

- A network has been created with important industries, thanks to the relationship with **FEDERCHIMICA** (Italian Federation of Chemical Industries), **CEFIC** (European Chemical Industries Council), as well as local and national **authorities**.
- **European authorities and agencies** have also been contacted, as well as the authorities of China, Taiwan, Canada and Japan .
- We have evaluated data provided by FEDERCHIMICA to analyze the impact of REACH on **PBT** and **CMR substances** in the Italian market for the time frame of from 2011 to 2020.
- We explored the **socio-economic impacts** of the implementation of in silico toxicology tools (its) in the R&D of European chemical companies, as they have the real opportunity to meet the ever-increasing legislative requirements and improve knowledge of toxic properties of the substances investigated, quickly and at low cost.
- To give some examples of the **private companies** from the different **industrial sectors** with which contacts were established during the project, we can cite ALCEA S.P.A., C.O.I.M. S.P.A., Chimiver Panseri s.p.a. Colorgraf s.p.a. Dumax s.r.l. Industrie chimiche forestali (ICF), Durante Adesivi S.P.A. Elantas Europe s.r.l., Fratelli Zucchini s.p.a., HUBER group Italia s.p.a., Icro Coatings s.p.a., Sunchemical, Flint Group, IVAS Industria VernicI s.p.a., Kerakoll s.p.a., Lechler s.p.a., Metlac s.p.a., N.P.T. S.R.L., Palini Vernici s.r.l., Savare' I.C. S.R.L., Saint-Gobain Italia s.p.a., Salchi Metalcoat s.r.l, Sestriere Vernici s.r.l, Sirca s.p.a., Verinlegno s.p.a., Von Roll Italia s.R.L. as well as a few sectorial grouping within FEDERCHIMICA (e.g., **MAPIC**, representing the Cosmetic Raw Materials producers, and **AVISA**, being the Italian Association representing adhesives, sealants, paints, varnishes and printing inks' producers)

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