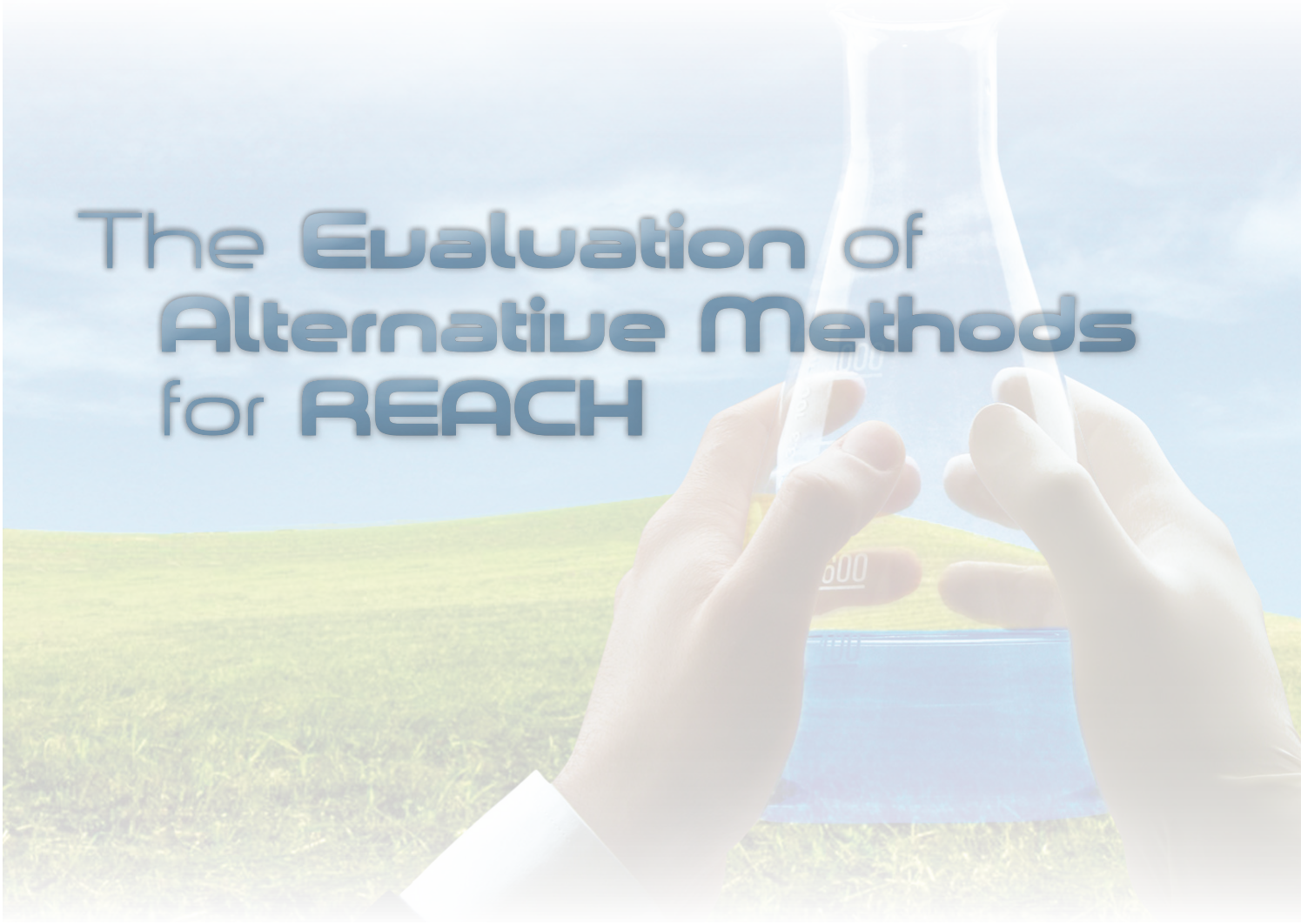
antares

Alternative Non-Testing methods
Assessed for REACH Substances

The Evaluation of Alternative Methods for REACH



LAYMAN'S REPORT

www.antares-life.eu

Alternative Non-Testing methods Assessed for REACH Substances

Contents

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Introduction
The REGULATION ON CHEMICALS and ALTERNATIVE METHODS

In order to ensure higher safety of chemical compounds and consequently a lower impact of these on human health and the environment, the European Union has introduced a new legislation for chemicals, **REACH** (**Registration, Evaluation, Authorisation and Restriction of Chemical substances - Regulation (EC) No.1907/2006** in force since June 1, 2007); it requires that all chemicals produced and/or placed on the EU market in quantities greater than or equal to 1 ton/year have appropriate safety information; in fact for each substance the industry is obliged to prepare a dossier containing information on physico-chemical, toxicological and ecotoxicological properties, to be sent to the **European Chemicals Agency** (**ECHA**) in order to obtain the registration and the subsequent authorization to manufacture and/or import.

REACH has therefore induced an urgent demand of toxicity tests for a large number of chemicals; the initial estimates talked about 100,000 registered substances for REACH by 2018, the year of the last deadline given by the regulation.
To meet these requirements, REACH provides that alternative methods to the use of animals (the so-called *in vivo* methods) shall be used, including **Non-Testing Methods** (**NTM**), able to predict the effects of the substance without its direct use but only on the basis of its structure (Art.13 of REACH). Indeed REACH, in addition to provide an increase in the level of protection of human health and the environment against the risks related to chemicals, has among its main objectives the promotion of alternative methods for the assessment of hazards deriving from chemical substances (Art.1 of REACH).

Examples of alternative methods, both included in the larger category of *in silico* methods (methods that use computer simulation or computer modeling to predict and evaluate the toxicological properties of a chemical on people and environment) are **(Q)SAR models** and **read-across**:

- a **(Q)SAR model** (**Quantitative Structure-Activity Relationship**) is a mathematical relationship that correlates one or more quantitative parameters derived from the chemical structure of the substance to quantitative or qualitative measure of a chemical property or biological activity (such as toxicity).
- **"to do read-across"** refers instead to the use of information related to a particular property or effect of one or more studied compounds for another compound considered similar, allowing to identify groups or categories of substances that share similar characteristics.

Before carrying out experiments on animals, to be considered as a last resource of information on the toxicity of chemicals (Art.25 of REACH), the chemical industry should verify if alternative methods exist; however still remain gaps today in the knowledge about what methods are available and can be used in practice.

http://echa.europa.eu/legislation/reach_legislation_en.asp

Purpose and Main Objectives of the LIFE+ project ANTARES

The main aim of the **ANTARES** (**Alternative Non Testing methods Assessed for REACH Substances**) project was to reduce the gaps in knowledge concerning the NTM methods, promoting them for their own use under REACH, linking scientists, regulators and industry in achieving this goal.
ANTARES therefore has been intended to assess and validate existing NTM methods (it has not implied the development of new tools, aiming to valorize those already available), in particular (Q)SAR, in order to allow their application for regulatory purposes.

Promotion of Non-Testing Methods (NTM) for their use in the REACH context linking scientists, regulators and industries

to EVALUATE and VALIDATE existing NTM for their application according to REACH NEEDS

Article 1 of REACH

This Regulation should ensure a *high level of protection of human health and the environment* as well as the free movement of substances in preparations and in articles, while *enhancing competitiveness and innovation.*

This Regulation *should also promote the development of alternative methods* for the assessment of hazards of substances.

Specific expected **OBJECTIVES** are:

1. to verify the possible use and performance of the existing NTM for REACH.
2. to identify requirements and constraints originating from the REACH legislation about the use of NTM.
3. to identify safety assessment factors for the NTM in order to increase their reliability.
4. to identify the best applicability for a safer use of the NTM.
5. to integrate different NTM achieving superior performance.
6. to disseminate the results.
7. to promote NTM for legislative purposes.

http://www.antares-life.eu/reach-ntm.php

WHY to use NTM tools for REACH purposes

The availability of evaluated and validated **Non-Testing Methods** (**NTM**) will lead to an increase in the protection of human health and the environment, providing models for testing the toxicity of chemical compounds that offer several advantages compared to *in vivo* methods because:

• THEY ARE INNOVATIVE

The theme of innovation is clearly mentioned in the REACH Regulation. The current models are not sufficient to cover the requests for information and it is necessary to develop and use new methods. ANTARES has achieved, among others, the objective to develop a new platform that includes various NTM models (**VEGA - Virtual models for property Evaluation of chemicals within a Global Architecture**, available at www.vega-qsar.eu).
Moreover, the innovation of using NTM represents a necessity because in Europe there's a lack of laboratories able to perform the tests required by REACH.
ANTARES has promoted new resources, partnerships and networks of contacts; in collaboration with the Italian authorities for REACH a network of specialized laboratories in (Q)SAR methods has been established.

• THEY DON'T INVOLVE USE OF ANIMALS

Animal testing is an argument that implies ethical issues deeply felt in Europe. The availability and usefulness of *in silico* methods would lead to a decrease in the number of animals (millions) used to perform tests required by REACH.

• THEY ARE CHEAPER

The costs of the tests (billions of euro) are a serious problem for the industry, especially for SMEs (small and medium enterprises). The use of *in silico* models considerably reduces the costs for registrants of chemicals, ANTARES has proposed low cost solutions or completely free.

• THEY ARE FASTER

Time requested to get results of animal testing is often too long to quickly protect people and environment. The industry has the need to obtain data in a short time to meet the deadlines imposed by the REACH Regulation. Thanks to NTM, thousands of chemical compounds can be analyzed in few days.

WHY to use NTM tools for REACH purposes

• THEY ARE STRATEGIC FOR INDUSTRY

Before marketing industry has the possibility of preliminarly evaluate chemical compounds that intends to produce and sell, through the use of NTM. The possibility to perform a preliminary screening on the basis of NTM could lead to choose safer substances, for example in case you want to proceed to the synthesis of a new compound, or if you need to evaluate the import of several substances from extra-EU.

• THEY STIMULATE THE RESEARCH FOR "GREEN" CHEMICALS WITH A LIMITED ENVIRONMENTAL IMPACT

The *a priori* evaluation of the toxicity of a compound, allowing "to plan" safer productions, leads to a reduction of the impact of chemicals on the environment. The NTM methods are also safer than *in vivo* testing because they don't produce waste or emissions or imply risk of accidents; they're virtual models.

• THEY CAN BE USED FOR THE CLASSIFICATION AND PRIORITIZATION OF CHEMICALS

Non-Testing Methods can be used under REACH not only to produce data for the preparation of the registration dossier but also to derive deductions for the purposes of correct classification and prioritization of chemicals. REACH requires to prioritize chemicals; today the authorities are able to control only 5% of the compounds (for each registration deadline foreseen by REACH) and in silico methods provide valid tools to order chemicals according to their degree of toxicity (identification of a compound, for example, as carcinogenic, mutagenic, toxic to reproduction, persistent, bioaccumulative, very persistent, very bioaccumulative).

Work plan and ACTIONS of the project

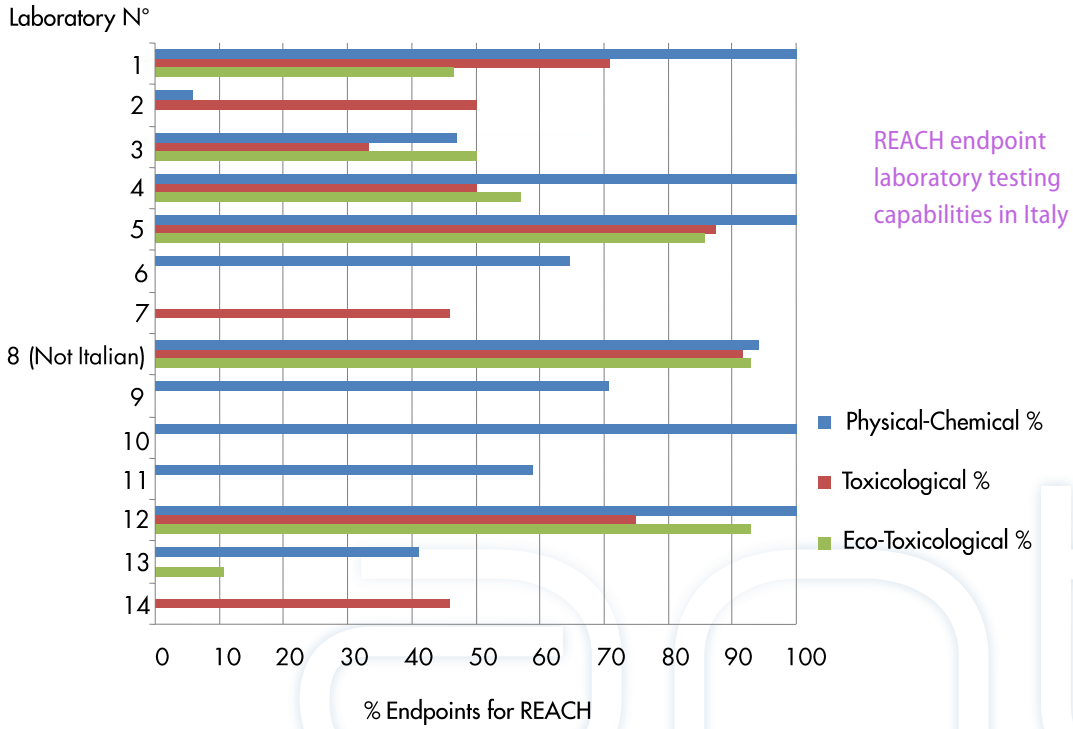
The project, lasting 36 months, began January 1, 2010 and ended December 31, 2012; it was characterized by a work plan divided into **13 Actions**:

- ***Action 1***
  Survey of current methods for compliance to REACH legislation
- ***Action 2***
  Identification of criteria for non-testing methods for REACH legislation
- ***Action 3***
  Identification of suitable experimental databases/data sets for ecotoxicological, toxicological and environmental endpoints
- ***Action 4***
  List of (Q)SAR models for ecotoxicological, toxicological and environmental endpoints for REACH, and their review
- ***Action 5***
  Validation of non-testing methods
- ***Action 6***
  Identification of boundaries for best use of models (applicability domain) and of the assessment factors
- ***Action 7***
  Architecture for integration of different non-testing methods for best performances and coverage of applicability
- ***Action 8*** Communication and Dissemination
- ***Action 9*** Web Portal
- ***Action 10*** Project Management
- ***Action 11*** Monitoring
- ***Action 12*** Audit
- ***Action 13*** After-LIFE Communication plan

http://www.antares-life.eu/actions.php

RESULTS of the PROJECT

At the beginning of the project **a survey was conducted aimed to assess the ability of laboratories to perform the tests required by REACH, the costs requested for the execution of tests and the number of animals used for each of them**.
For this purpose some Italian laboratories and an European one have been contacted, verifying the degree of correspondence between the tests they offer and those required by REACH.



If the first registration deadline imposed by the REACH Regulation (30 November 2010) involved substances with already existing experimental data, the second (31 May 2013) and third registration deadlines (31 May 2018) will cover a large number of substances that require new studies; viewing the graph you may imagine that there are test-capacity limits of laboratories which cooperated in the survey.

Continuing, **the average costs of the tests offered by the Italian laboratories have been analyzed and have been also compared to those of German laboratories**, on the basis of a survey conducted by the German Chemical Industry Association (VCI - Verband der Chemischen Industries) often used in Europe as a reference in discussions concerning the activities of REACH registration.

The reference document (**Deliverable 1**) can be downloaded from the project website (http://ww.antares-life.eu/action1.php) but below there are few examples that show how the costs that the industry has to pay for toxicity tests often prove prohibitive:

Example of average costs of tests offered by German (VCI) and Italian laboratories

RIF. REACH	ENDPOINT	Guide-line	#	Mean VCI [€]	MEAN Italian Labs [€]
8.	**TOXICOLOGICAL INFORMATION**				
8.7.3	Two-Generation Reproduction Toxicity study	OECD	416	305.000	259.000
8.9	**Carcinogenicity study**	OECD	451	630.000	800.000

Animal testing for the first REACH registration deadline has been extremely limited in order to respect the ECHA disposition to transmit only testing proposals (then evaluated by the Agency) in case of lack of experimental data. For this reason, only limited information about the real use of *in vivo* tests has been collected; however, **a list with the potential number of animals used for each REACH test** has been published.

Example of the potential number of animals used for REACH tests

RIF. REACH	ENDPOINT	Guide-Line	#	Endpoint	Pref. Species	Stage	Route	Frequency	Duration (d)	Test Duration (d)	Test Groups	Animals/Group	Test Animals	Pups	Animals (+pups) total
8.7.3	Two-Generation Reproduction Toxicity study	OECD	416	NOAEL	Rat	Adult	Oral	Daily	Point/Semi-continous (84F1m/130F1f)	260?	3 + Control	40 (20f/20m)	160 (F1) + 160 (F2)	1760	2080
8.9.1	Carcinogenicity Studies	OECD	451	NOAEL	Rat + Mice	(Post)Weanling	Oral/Dermal/Inhalation	Daily	Point/Semi-continous	730 r & 548 m	3 + Control	100 (50f/50m)	400	0	400
	Chronic Toxicity Studies	OECD	452	NOAEL	Rat + non-rodent	Post-Weanling	Oral/Dermal/Inhalation	Daily	Point/Semi-continuous	365	3 + Control	40 (20f/20m)	120	0	120
	Combined Chronic Toxicity/Carcinogenicity Studies	OECD	453	NOAEL	Rat + non-rodent	(Post)Weanling	Oral/Dermal/Inhalation	Daily	Point/Semi-continuous	730 r & 548 m	3 + Control	100 (50f/50m)	400	0	400

Considering the results above it can be therefore concluded that **the use of NTM methods represents almost a necessity** to cope with economic and ethical problems associated to *in vivo* methods as well as inability of laboratories to provide all the types of tests required by REACH.

However, there are **barriers** for which today the NTM are not widely used in industry for the production of toxicological data; regarding this matter, during a survey aimed at checking the knowledge, habits, opinions, expectations of laboratories, consultants, authorities and industries with regard to NTM, some chemical companies have completed a questionnaire in order to determine whether, during the first phase of REACH registration, NTM methods had been used for the preparation of dossiers and to understand what were the major obstacles that didn't allow their use; the greater obstacle found is represented by the low propensity of Regulators to accept data derived from NTM methods, to which is added the fact there's only a limited number of methods actually usable by industry.

The **acceptability by Regulators of the results provided by NTM methods** is the key passage to ensure their wide applicability in the future.

Thus, it appears clear that there's a need **to characterize the NTM methods available in order to increase their acceptability by Regulators;** to do this, one of the first steps to take is certainly to evaluate and compare NTM methods in order to use those which provide better results and, above all, usable under REACH (ie registration, classification, prioritization of chemicals).

Therefore, in the context of the project, for this purpose, **an assessment system has been established based on a set of criteria** (divided into primary and additional, depending on their importance) useful to identify, among the existing ones, (Q)SAR models which might be considered for REACH purposes and to choose the best model in case several models for the study of a single endpoint result to be available (http://www.antares-life.eu/action2.php). A score is assigned to each criterion; the best models are those that, following the evaluation, achieve the highest score for each criterion.

Before the evaluation and comparison of different NTM methods is necessary, however, **to have experimental data on toxicity, ecotoxicity, physico-chemical and environmental properties of chemicals**, which is the basis for the use of read-across methods and (Q)SAR models: only through the comparison with the experimental value it can be deducted if a value predicted by an NTM is reliable or not. For this reason, the quality and appropriateness of databases for REACH purposes are critical.
In this regard, **databases useful for the requirements of the REACH Regulation** and therefore suitable for REACH endpoints, have been identified during the project. Various databases have been analyzed, starting from IUCLID (used by ECHA) and then going through the examination of others, with preference for those freely accessible, as OECD ToolBox, DSSTox, Actor, Osiris, ISSCAN, etc.
In these cases evaluation criteria have been adopted whether a database could be considered usable or not for REACH endpoints (http://www.antares-life.eu/action3.php).

Then proceeding, existing and usable (Q)SAR models for REACH endpoints have been identified; they have been evaluated according to the system based on the criteria mentioned above as well as on the basis of test results coming from a range of industrial chemicals.

These actions led **to validate some model** and to choose those that meet the requirements given by REACH. The performance of the models has been measured through mathematical and statistical analysis, limits and applicability domains (ie the group of compounds for which a model provides reliable results) of each model considered valid have been identified; integration studies finally allowed to understand how to get best results thanks to the combination of different models.

Ultimately, t**he project has allowed therefore to make a number of (Q)SAR models available and usable to study physico-chemical, toxicological, ecotoxicological and environmental properties of chemicals**.
It was not possible to validate models for all REACH endpoints, but for a lot of them (Q)SAR models can be used, and for some of them several models are available, as shown in the following **tables**:

Endpoints for REACH considered within ANTARES and related available (Q)SAR models

ENDPOINTS	MODELS
7.1. State at 20°C and 101,3 kPa	-
7.2. Melting/freezing point	++
7.3. Boiling point	++
7.4. Relative density	+
7.5. Vapour pressure	++
7.6. Surface tension	+
7.7. Water solubility	++
7.8. Partition Coefficient n-octanol/water	++
7.9. Flash-point	+
7.10. Flammability	+
7.11. Explosive properties	-
7.12. Self-ignition temperature	-
7.13. Oxidising properties	-
7.14. Granulometry	-
7.15. Stability in organic solvents ..	-
7.16. Dissociation constant	++
7.17. Viscosity	+

YELLOW: PHYS-CHEM PROPERTIES;
ORANGE: TOXICOLOGICAL PROPERTIES;

- no suitable models;
+ some suitable models;
++ a certain number of models.

ENDPOINTS	MODELS
8.1. Skin irritation or skin corrosion	
8.1.1. in-vivo skin irritation	+
8.2. Eye irritation	
8.2.1. in-vivo eye irritation	+
8.3. Skin sensitisation	++
8.4. Mutagenicity	
8.4.1. In-vitro gene mutation study in bacteria	++
8.4.2. In-vitro cytogenecity or micronucleus study in mamm. cells	-
8.4.3. In-vitro gene mutation study in mammalian cells	-
8.4.4. In-vivo mutagenicity study	+
8.5. Acute toxicity	
8.5.1. Acute toxicity - by oral route	++
8.5.2. Acute toxicity - by inhalation	+
8.5.3. Acute toxicity - by dermal route	-
8.6. Repeated dose toxicity	+
8.6.1. Short-term repeated dose toxicity (28 d)	+
8.6.2. Sub-chronic toxicity study (90 days)	+
8.6.3. A long-term repeated dose toxicity (> 12 m)	-
8.7. Reproductive toxicity	++
8.7.1. Screening for reproductive-/developmental toxicity	-
8.7.2. Pre-natal developmental toxicity study	-
8.7.3. Two-generation reproductive toxicity study	-
8.8. Toxicokinetics	++
8.8.1. Assessment of the toxicokinetic	-
8.9.1. Carcinogenicity study	++

ENDPOINTS	MODELS
9.1. Aquatic toxicity	
9.1.1. short-term toxicity testing on invertebrates (Daphnia)	++
9.1.2. Growth inhibition study aquatic plants (Algae preferred)	+
9.1.3. short-term toxicity testing on fish	++
9.1.4. Activated sludge respiration inhibition testing	+
9.1.5. Long-term toxicity testing on invertebrates (preferred Daphnia)	+
9.1.6. long-term toxicity testing on fish	+
9.1.6.1. Fish early-life stage (FELS) toxicity test	-
9.1.6.2. Fish short-term toxicity test on embryo and sac-fry stages	-
9.1.6.3. Fish, juvenile growth test	-
9.4. Effects on terrestrial organisms	-
9.4.1. short-term toxicity to invertebrates	-
9.4.2. Effects on soil micro-organisms	-
9.4.3. short-term toxicity to plants	-
9.4.4. Long-term toxicity testing on invertebrates	-
9.4.6. Long-term toxicity testing on plants	-
9.5.1. Long-term toxicity to sediment organisms	-
9.6.1. Long-term or reproductive toxicity to birds	-

ENDPOINTS	MODELS
9.2. Degradation	
9.2.1. Biotic	
9.2.1.1. Ready biodegradability	++
9.2.1.2. Simulation testing on ultimate degradation in surface water	-
9.2.1.3. Soil simulation testing	-
9.2.1.4. Sediment simulation testing	-
9.2.2. Abiotic	
9.2.2.1. Hydrolysis as a function of pH	+
9.2.3. Identification of degradation products	+
9.3. Fate and behaviour in the environment	
9.3.1. Adsorption/desorption Screening	+
9.3.2. Bioaccumulation in aquatic species, preferably fish	++
9.3.3. Further information on adsorption/desorption	-
9.3.4. Info on the environ. fate and behaviour of the substance	-

BLUE: ECOTOXICOLOGICAL PROPERTIES;
GREEN: ENVIRONMENTAL PROPERTIES.

- no suitable models;
+ some models;
++ a certain number of models.

Different (Q)SAR models for the prediction of the properties of chemical compounds are the functional basis of **various softwares collected by ANTARES and available on project website** (http://www.antares-life.eu/software.php); for each REACH endpoint several usable software can exist, some of them are freely accessible while others are commercial.

Between the available softwares, **VEGA** (**Virtual models for property Evaluation of chemicals within a Global Architecture** - www.vega-qsar.eu) has been developed within the ANTARES project; VEGA is a platform that integrates (Q)SAR models and read-across and allows experts to make a prediction of the characteristics of substances of interest in relation to some REACH endpoints.

The Home page of the VEGA website

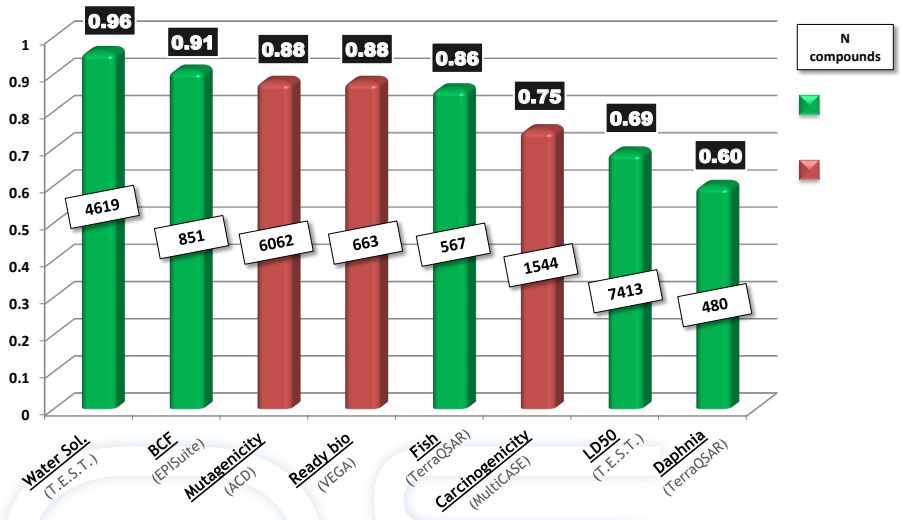
The VEGA software is free and downloadable at http://www.vega-qsar.eu/download.html after web site registration.

The web page where the VEGA software can be downloaded

A more detailed study on the **real predictability of NTM** has been conducted for **eight properties**, interesting from the point of view of the **human toxicology**, **ecotoxicology**, **environmental** and **physico-chemical properties**, as indicated in this table.

Mutagenicity (Ames)	HUMAN TOXICITY
Carcinogenicity	
LD50	
Fish Acute Toxicity	ECOTOXICOLOGY
Daphnia Acute Toxicity	
BCF	ENVIRONMENTAL PROPERTIES
Ready Biodegradability	
Water Solubility	PHYSICO-CHEMICAL PROPERTIES

The results of more than 50 NTM models have been used to obtain an **overall picture of the ability of each model to correctly predict the properties studied**. The following graph shows the best results that have been achieved.



Overall values were about 22,000 points, and this is a broad-based assessment.

However this framework can be partial: it is possible that the results appear to be good not because the model is predictive, but because the data of several compounds is already known to the developers of the model. Therefore, ANTARES has duly verified the performance of individual models only considering compounds really new, never used to build the model. In these conditions, the results generally get worse.

Moreover ANTARES has taken into account the assessment provided by the model on the reliability of the prediction in relation to the use of the model for a certain compound. In this way, it has been considered the applicability domain of each model. It is likely that a certain model cannot not be predictive for all substances, but it works better for certain compounds.
It was verified that the models are generally capable to assess whether a prediction is reliable or not. Taking this into account the results generally improve. For example, for mutagenicity (Ames Test), the accuracy of prediction has been proved to be very good. Good results have been also obtained for the water solubility.

It should also be said that there are properties for which the reliability of the models is more limited, and the use of the models should be adopted only on well specified chemical classes, and using more than one combined model. The use of models to predict the carcinogenicity can't be an alternative to replace the traditional method, but however the information provided by the model can be a useful complement to the overall assessment of the substance.

In the environmental field, the best models were those for persistence. Moreover, there are useful perspectives for models on bioaccumulation while aquatic toxicity, especially towards the daphnia, shows problems, probably due to some uncertainty of the experimental data.

TRANSFERABILITY of RESULTS

The best models analyzed in the context of the ANTARES project will be used to study certain properties of chemical substances already registered under REACH (for which toxicity data are therefore already available) thanks to a new LIFE project, CALEIDOS, which began on January 1, 2013.

CALEIDOS (Chemical Assessment according to Legislation Enhancing the In silico Documentation and Safe use) will evaluate the real usability of *in silico* models validated by ANTARES, checking if they're able to provide results comparable to those already submitted to ECHA for the registration of the substances tested.

http://www.caleidos-life.eu

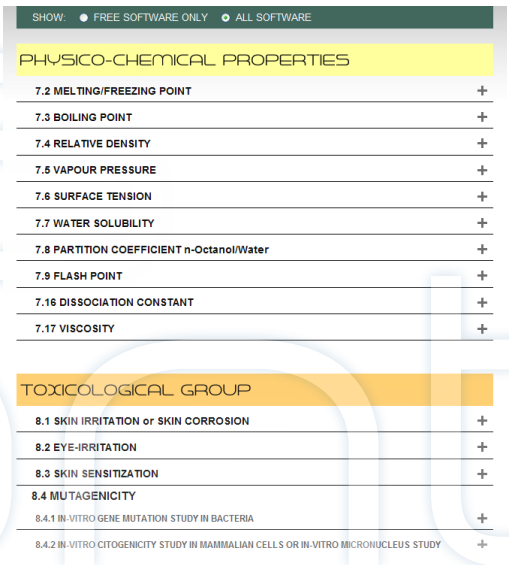
In a wider context, characterization and validation of Non-Testing Methods within ANTARES represents a real boost to the effective reduction of animal experiments, which currently are also widely used by other industrial sectors, such as pharmaceutical; pharmaceutical industry requires about half of the animals annually used in Europe for toxicological tests.

The PROJECT WEB PORTAL

Information about the Actions and results of ANTARES are available on the project website: www.antares-life.eu.

The ANTARES site, active for 5 years after the end of the project, is organized into the following main **sections**:

- EVENTS
  Information on initiatives related to the project such as seminars, workshops, meetings, training sessions, meetings with regulators and industry.
- RESOURCES
  Reports, brochures, newsletters, presentations, posters.
- SOFTWARE
  Software available for each endpoint REACH.
- E-LEARNING
  Teaching material for the understanding of (Q)SARs, suitable for students and non-experts.



The Project BENEFICIARIES

1 Istituto di Ricerche Farmacologiche Mario Negri (Coordinator)

The MARIO NEGRI INSTITUTE FOR PHARMACOLOGICAL RESEARCH (IRFMN) is a not-for-profit biomedical research organization, founded in Milan in 1961, with research units also in Bergamo, at Ranica – near Bergamo – and at Santa Maria Imbaro, near Chieti. The Institute's main aim is to help defend human health and life.

The *Laboratory of Environmental Chemistry and Toxicology* at IRFMN is coordinating/coordinated in the past 15 EC projects, and is participating, or has participated, to 18 other EC projects.

These projects deal with (Q)SAR, toxicity, Information Technologies, dissemination of knowledge and results and integration of knowledge.

Within one of these projects, CAESAR, a software platform has been developed including available (Q)SAR models for REACH.

Within the project DEMETRA, a new software for regulatory purposes for pesticides has been developed.

2 Istituto Superiore di Sanità

The ISTITUTO SUPERIORE DI SANITÀ (ISS), established in Rome, is the leading technical and scientific public body of the Italian National Health Service.

Its activities include research, control, training and consultation in the interest of public health protection.

The Institute conducts scientific research in a wide variety of fields, from cutting-edge molecular and genetic research to population-based studies of risk factors for disease and disability. Research priorities are based on those set forth in the National Health Plan.

3 Federchimica

FEDERCHIMICA is the abbreviated name of the ITALIAN FEDERATION OF THE CHEMICAL INDUSTRY, founded in 1920. At the present time 1,300 companies, with a total of 94,000 employees, are part of Federchimica. They are grouped into 16 Associations, which in turn are subdivided into 43 product groups. Federchimica is a member of Confindustria (General Confederation of the Italian Industry) and CEFIC (European Chemical Industry Council). Its primary objectives are the coordination and the protection of the role of the Italian chemical industry as well as the promotion of its development capacity.

The Project BENEFICIARIES

4 POLITECNICO DI MILANO

The POLITECNICO DI MILANO University was established in 1863 and it is now ranked as one of the most outstanding European universities in Engineering, Architecture and Industrial Design.
The *Department of Electronics and Information* of the Politecnico di Milano is a unique environment that blends competences and disciplines usually mapped in separate CS and EE departments.
At DEI cross-fertilization is a working reality where researchers are eager to tackle complex and challenging problems, contributing to shape key achievements in computer engineering, telecommunications, systems and control, electronics.

POLITECNICO DI MILANO

5 KNOWLEDGEMINER SOFTWARE

The KNOWLEDGEMINER SOFTWARE is a German privately held company in the field of research, consulting, development, and application of unique self-organising, inductive, knowledge discovery technologies.
The company developed the KnowledgeMiner® software package, a distinguished commercial self-organising modelling tool.
It implements an innovative set of high-performance parallel algorithms for modelling and validation of complex systems to allow knowledge extraction from noisy data in a most objective and automated way.

KnowledgeMiner Software

Alternative Non-Testing methods Assessed for REACH Substances

www.antares-life.eu

info@antares-life.eu

The LIFE Programme

LIFE (**L'I**nstrument **F**inancier pour l'**E**nvironnement) is ***the EU's funding instrument for the environment***, launched by the European Commission and coordinated by the Environment Directorate-General.
The general objective of LIFE is to contribute to the implementation, updating and development of EU environmental policy and legislation by co-financing pilot or demonstration projects with European added value.

LIFE began in 1992 and to date there have been three complete phases of the programme (LIFE I: 1992-1995, LIFE II: 1996-1999 and LIFE III: 2000-2006). During this period, LIFE has co-financed some 3104 projects across the EU, contributing approximately €2.2 billion to the protection of the environment.

LIFE+ The current phase of the programme, LIFE+, runs from 2007-2013 and has a budget of €2.143 billion. The legal basis for LIFE+ is the Regulation (EC) No 614/2007. LIFE+ covers both the operational expenditure of DG Environment and the co-financing of projects. According to Article 6 of the LIFE+ Regulation, at least 78 percent of the LIFE+ budgetary resources must be used for project action grants (i.e. LIFE+ projects).
During the period 2007-2013, the European Commission will launch one call for LIFE+ project proposals per year.

The ANTARES project has been declared eligible under the programme component LIFE+ Environment Policy and Governance.

The **Environment Policy & Governance** component continues and extends the former LIFE Environment programme. It will co-finance innovative or pilot projects that contribute to the implementation of European environmental policy and the development of innovative policy ideas, technologies, methods and instruments. It will also help monitor pressures (including the long-term monitoring of forests and environmental interactions) on our environment.

http://ec.europa.eu/environment/life/about/index.htm

Alternative Non-Testing methods Assessed for REACH Substances

LIFE08 ENV/IT/00435