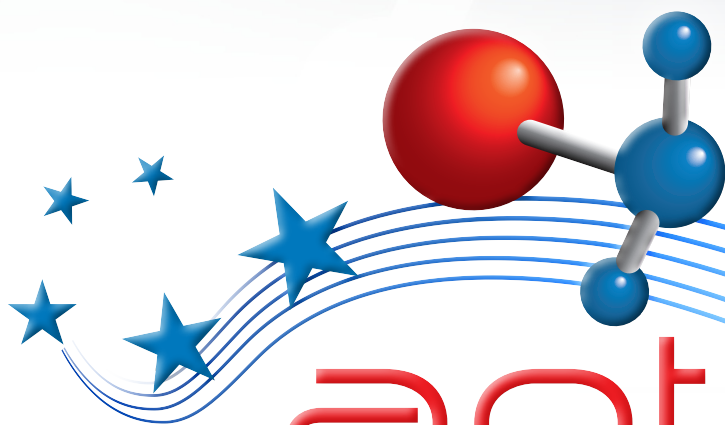


Welcome to



antares

Alternative Non-Testing methods
Assessed for REACH Substances

Introduction
to the Project

www.antares-life.eu



Alternative Non-Testing methods Assessed for REACH Substances



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The REACH legislation requires that all chemicals present in the European market in an amount higher than 1 t/year have suitable safety information

EC REGULATION No 1907/2006 - Registration, Evaluation, Authorisation and restriction of Chemicals

REACH states that Non-Testing Methods (NTM) can be used to fulfill this requirement

Before making an animal experiment the industry should verify if *alternative methods* exist.

The *NTM methods* are examples of alternative methods which predict the effects of chemicals without the use of the real compound, but only on the basis of the compound structure. They include *Quantitative Structure-Activity Relationship (QSAR) models* and *Read-Across*.

However, so far there is a *gap of knowledge* on which methods are available and can be used in practice.

The ANTARES project aims to reduce this gap assessing NTM as an alternative approach for the REACH legislation.

The **MAIN OBJECTIVES** of ANTARES are:

- to verify the possible USE and PERFORMANCE of the NTM for REACH;
- to identify REQUIREMENTS and CONSTRAINTS originating from the REACH legislation;
- to identify SAFETY ASSESSMENT FACTORS for the NTM;
- to identify the BEST APPLICABILITY for a safer use of the NTM;
- to INTEGRATE DIFFERENT NTM achieving superior performance;
- to DISSEMINATE the results;
- to PROMOTE NTM for legislative purposes.

The main result will be a CHARACTERIZATION of the NON- TESTING METHODS suitable for REACH



ANTARES is organized in **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

see Page 8

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

see Pages 6-9

Action 10 Project Management

Action 11 Monitoring

Action 12 Audit

Action 13 After-LIFE Communication plan

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



REACH and NON-TESTING METHODS



**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.

ANTARES is going on with the evaluation and assessment of the available NTM, in particular *Quantitative Structure-Activity Relationship (QSAR) models*, and the promotion of new tools and resources.

<http://www.antes-life.eu/reach-ntm.php>
http://echa.europa.eu/legislation/reach_legislation_en.asp



QSAR tools for REACH purposes can be used for SEVEN REASONS

Innovative tools

Time for experiments

Occurrence of enough laboratories/resources

Reduction of costs

Use of animals

Prioritization needs

Pro-active approach for greener chemicals



For each of them we can identify the CURRENT CRITICAL ISSUES and propose SOLUTIONS through ANTARES

1. INNOVATIVE TOOLS



- ❓ Current methods are not sufficient. Innovation is clearly mentioned within the REACH legislation.
- + ANTARES promotes a new platform wrapping several models:
VEGA - Virtual models for property Evaluation of chemicals within a Global Architecture

<http://www.vega-qsar.eu>

2. TIME FOR EXPERIMENTS



- ❓ The time requested to produce with *in vivo* methods all the data required by REACH would be very long. Industry faces long time to get the experimental values.
- + ANTARES promotes faster tools, e.g. through the VEGA platform.

3. OCCURRENCE OF ENOUGH LABORATORIES/RESOURCES



- ❓ As highlighted in the ANTARES Action 1, in Europe there is a lack of laboratories capable to perform tests requested by REACH.

<http://www.antares-life.eu/action1.php>

- + ANTARES promotes new resources, collaboration and networking. With Italian Authorities for REACH a NETWORK OF LABORATORIES expert on QSARs has been identified.

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

4. REDUCTION OF COSTS



- ❓ Costs for experiments would be billions of euros and a huge problem for SMEs. Part of them could be avoided using cheaper *in silico* methods.
- + ANTARES promotes cheap and /or free solutions.

5. USE OF ANIMALS



- ❓ The usage of animals is a strong ethical issue in Europe. REACH requires using millions of animals: part of them could be avoided through *in silico* methods.
- + ANTARES promotes non-animal testing.

6. PRIORITIZATION NEEDS



- ❓ REACH requires prioritizing chemicals. Today authorities are capable to check 5% of chemicals. *In silico* methods offer tools to sort them according to their toxicity.
- + ANTARES promotes tools suitable for prioritisation (VEGA), and Italian regulators are interested in these tools.

7. PRO-ACTIVE APPROACH FOR GREENER CHEMICALS



- ❓ So far chemicals have been prepared and toxicity has been discovered later. Safer and "greener" products need to be designed since the beginning.
- + ANTARES supports tools for safer chemicals, in contact with selected industries.



ANTARES WEB PORTAL OVERVIEW

The ANTARES project deals with innovative technologies and advanced interactive tools.

This implies an active and propulsive presence in the Internet, with an *updated and easy-to-use web site*.

www.antes-life.eu

The ANTARES Web Portal is aimed to provide the user with a *prompt information about the project activities and the development itself of the project*, just from the *Home page* through a visual code which gives an *immediate overview of the state-of-the-art of the Actions*.

The status and results of each action are regularly updated, with *public related documents uploaded to the website* as downloadable resource and/or as specific website sections.

Latest *News* about the project's results, as well as about *in silico* approaches related news, events and resources are frequently published and highlighted.



ON GOING Action



ACCOMPLISHED Action



NOT STARTED Action



SPOT ON

Models evaluated for REACH

38 endpoints covered

More than 250 software available

More than 70 are free

NEWS & EVENTS

eLEARNING: new section for learning QSARs is now open.

Monday, October 3rd, 2011

Italian Working group on QSAR and REACH launched by the *Ministero della Salute*

Friday, September 23rd, 2011

<http://www.antes-life.eu/index.php>
<http://www.antes-life.eu/actions.php>
<http://www.antes-life.eu/results.php>



The **SECTIONS** of the **WEB PORTAL**

The contents of the ANTARES Web Portal are organized in the following main sections:

EVENTS
RESOURCES
SOFTWARE
E-LEARNING

HOME

EVENTS

RESOURCES

SOFTWARE

eLEARNING

REACH & NTM

PLANNED ACTIVITIES

RESULTS

LIFE PROGRAMME

BENEFICIARIES

EVENTS

<http://www.antes-life.eu/events.php>

The EVENTS section includes all the events related to the activities of the ANTARES project, organized in the following sub-categories:

- **Seminars for the European regulatory bodies**
- **International events' participation**
- **Didactic courses and initiatives**
- **Events towards industry**
- **Workshops and seminars**
- **Meetings with national regulatory bodies**
- **Project meetings**

Seminars for the European regulatory bodies

SEP 13 2011	Copenhagen, Denmark Meeting at European Environment Agency (EEA) Participation: E. Benfenati & G. Gini
OCT 27 2010	Parma, Italy Meeting with EFSA, and presentation of the project ANTARES Participation: E. Benfenati, A. Roncaglioni & G. Gini
SEP 23 2010	Helsinki, Finland Meeting at ECHA, discussion about possible collaboration for joint activities on read-across Participation: E. Benfenati
JUN 29 2010	Helsinki, Finland Discussion at ECHA about ANTARES, with plenary talk Participation: E. Benfenati (with A. Roncaglioni, R. Knauf, G. Gini & F. Lemke) with the talk "Towards a safer and more transparent use of QSAR models for toxicity prediction"
JUN 28 2010	Helsinki, Finland Meeting with ECHA Participation: E. Benfenati, A. Roncaglioni, R. Knauf, G. Gini & F. Lemke

International events' participation

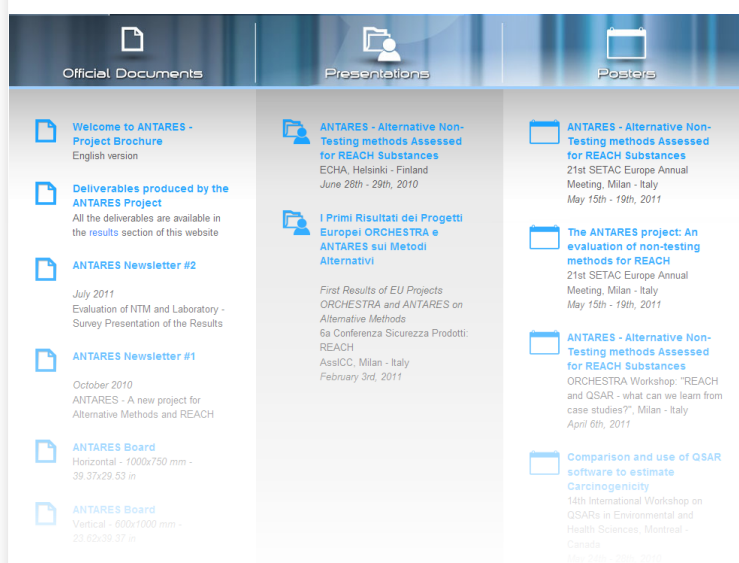
OCT 26-27 2011	Berlin, Germany 6th Meeting of the OECD QSAR Toolbox Management Group Participation: E. Benfenati, with a presentation of the VEGA platform
OCT 17-18 2011	Leipzig, Germany Expert Meeting of EUROECOTOX on the use of alternative methods Participation to the working groups: E. Benfenati



The SECTIONS of the WEB PORTAL

RESOURCES

<http://www.antes-life.eu/resources.php>



Official Documents

- Welcome to ANTARES - Project Brochure (English version)
- Deliverables produced by the ANTARES Project (All the deliverables are available in the results section of this website)
- ANTARES Newsletter #2 (July 2011: Evaluation of NTM and Laboratory - Survey Presentation of the Results)
- ANTARES Newsletter #1 (October 2010: ANTARES - A new project for Alternative Methods and REACH)
- ANTARES Board (Horizontal - 1000x750 mm - 39.37x29.53 in)
- ANTARES Board (Vertical - 600x1000 mm - 23.62x39.37 in)

Presentations

- ANTARES - Alternative Non-Testing methods Assessed for REACH Substances (ECHA, Helsinki - Finland, June 28th - 29th, 2010)
- I Primi Risultati dei Progetti Europei ORCHESTRA e ANTARES sui Metodi Alternativi (First Results of EU Projects ORCHESTRA and ANTARES on Alternative Methods, 6a Conferenza Sicurezza Prodotti: REACH, AssICC, Milan - Italy, February 3rd, 2011)

Posters

- ANTARES - Alternative Non-Testing methods Assessed for REACH Substances (21st SETAC Europe Annual Meeting, Milan - Italy, May 15th - 19th, 2011)
- The ANTARES project: An evaluation of non-testing methods for REACH (21st SETAC Europe Annual Meeting, Milan - Italy, May 15th - 19th, 2011)
- ANTARES - Alternative Non-Testing methods Assessed for REACH Substances (ORCHESTRA Workshop: "REACH and QSAR - what can we learn from case studies?", Milan - Italy, April 6th, 2011)
- Comparison and use of QSAR software to estimate Carcinogenicity (14th International Workshop on QSARs in Environmental and Health Sciences, Montreal - Canada, May 20th - 25th, 2010)

All the *public available documents* are uploaded in the RESOURCES section.

The resources have been organized in three sub-categories:

- **OFFICIAL DOCUMENTS** (deliverables, brochures, newsletters, boards, etc.)
- **PRESENTATIONS** given by ANTARES beneficiaries with acknowledgement to the project
- **POSTERS** about ANTARES

SOFTWARE

<http://www.antes-life.eu/software.php>

The SOFTWARE section has been implemented on the basis of the activities within Action 4 (*List of (Q)SAR models for the ecotoxicological, toxicological and environmental endpoints for REACH, and their review*) and includes a list of available resources (free and commercial software as well as articles regarding QSAR models) possibly usable for mostly all REACH endpoints.

This page allows the visualizing of the software available, as well as the type of software (both commercial and free or only free software) for each endpoint.

<http://www.antes-life.eu/action4.php>

SHOW: ☒ FREE SOFTWARE ONLY ☐ ALL SOFTWARE

PHYSICO-CHEMICAL PROPERTIES

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	+
7.16 DISSOCIATION CONSTANT	+
7.17 VISCOSITY	+

TOXICOLOGICAL GROUP

8.1 SKIN IRRITATION or SKIN CORROSION	+
8.2 EYE-IRRITATION	+
8.3 SKIN SENSITIZATION	+
8.4 MUTAGENICITY	+
8.4.1 IN-VITRO GENE MUTATION STUDY IN BACTERIA	+



The SECTIONS of the WEB PORTAL

E-LEARNING

<http://www.antaes-life.eu/learning.php>

The E-LEARNING section provides didactic material for understanding QSAR and is suitable for beginners and students allowing to download or view on-line presentations, e-book and other type of learning materials.

Contents are organized in six areas:



In the *Updates* page you can find the last articles posted on the blog.
In the sidebar there are a lot of useful links organized by categories.
Remember that to post comments you have to be registered to the site.

The *Introduction* section provides you general information about QSAR.
This section answers questions about what QSARs are, why using QSAR models and the relationship between QSAR and REACH European legislation.

The *Theory* page studies deeply mathematical and statistical aspects about QSAR. Here you can find algorithms and equations that describe how QSAR models work under the hood.

In the *How to Use* section there are useful video-presentation about practical use of the software in order to obtain chemical prediction.

In the *Online Resources* section you can find material like source code, software and other interesting links. Here practical aspects about QSAR models are described. Furthermore from here it is possible to download software and related tutorial to make your own predictions.

Finally in the *F.A.Q. (Frequently Asked Questions)* page you can interact with our staff. Your impressions about the site and the QSAR in general are very precious for us.



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 13 EC projects, and is participating, or has participated, to 17 other EC projects. These projects deal with QSAR, 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 QSAR 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 POLITECNICO DI MILANO



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.

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.

4 FEDERCHIMICA



FEDERCHIMICA
CONFINDUSTRIA

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.

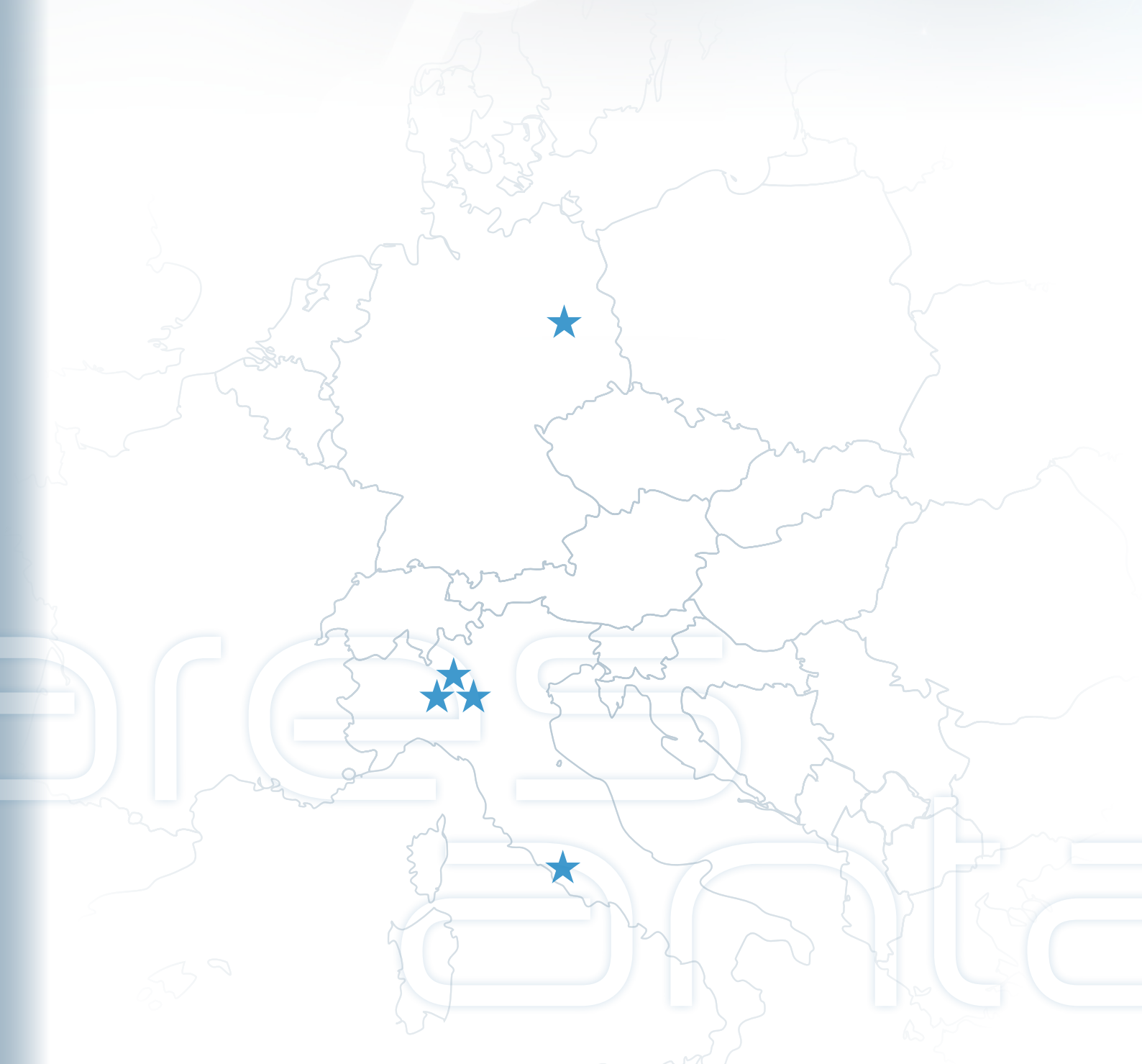
5 KNOWLEDGEMINER

The KNOWLEDGEMINER SOFTWARE is a German privately held company in the field of research, consulting, develop-



KnowledgeMiner
Software

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methods **A**ssessed for
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The **LIFE** Programme

LIFE (L'Instrument Financier pour l'Environnement) 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>

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**LIFE08
ENV/IT/00435**

