Summary
Authorization and restriction of chemicals (REACH) requires demonstration of the safe manufacture of chemicals and their safe use throughout the supply chain. REACH is based on the precautionary principle, but aims to achieve a proper balance between societal, economic and environmental objectives. Both new and existing chemicals will be evaluated within REACH, amongst others aiming to efficiently use the scarce and scattered information available on environmental fate and effects of chemicals. REACH thus aims at closing huge gaps of knowledge on physico-chemical properties and adverse effects of large numbers of chemicals. Thereupon REACH aims to reduce animal testing by optimized use of qualitative and quantitative information on related compounds. The REACH proposals advocate the use of non-animal testing methods, but guidance is needed on how these methods should be used.

It is within this context that CADASTER aims at providing the practical guidance to integrated risk assessment within REACH by performing a full hazard assessment for chemicals belonging to four compound classes. The main goal is to exemplify the integration of information, models and strategies for carrying out safety-, hazard- and risk assessments for large numbers of substances. Real risk estimates are delivered according to the basic philosophy of REACH of minimizing animal testing, costs, and time. CADASTER thus shows how to increase the use of non-testing information for regulatory decision whilst meeting the main challenge of quantifying and reducing uncertainty. On the basis of fusing the research findings with other ongoing research and regulatory developments, recommendations on a viable management strategy for optimized testing and in-silico modeling of hazardous organic chemicals, are provided. The focus of the activities was on assessing and quantifying uncertainty and variability in probabilistic risk assessment, as introduced by the use of non-testing information.
To achieve the main goals set for CADASTER, an intensive screening of the available experimental data and predictive (QSAR) models for endpoints relevant for risk assessment of the four chemical classes that were the topic of study within CADASTER, was initially performed. A subsequent gap analysis identified the most essential data and models that are lacking for performing future fate and effect assessment. Subsequent integration of the predictive tools thus obtained allowed for establishing a quantitative framework for integration of predictive tools within risk assessment. Case studies on a variety of endpoints relevant for chemical hazard and risk assessment for a blend of chemicals form within the four chemicals classes that were the topic of study within CADASTER, exemplified the application of testing alternatives and the subsequent uncertainties and variability. The case studies included:

- Assessing uncertainty and propagation of uncertainty in environmental fate modelling;
- ranking of compounds on the basis of their environmental hazard;
- ranking of compounds on the basis of their environmental risk, as calculated by combining effect assessment with fate assessment, whilst taking uncertainty and variability in input data into account;
- assessing uncertainties in risk assessment based on QSARs;
- applying read across approaches to chemical classes of a heterogeneous nature without much structural resemblance;
- prioritization based on evaluation of persistence, bioaccumulation potential and toxicity of chemicals and associate uncertainty analysis, and based on hazard assessment;
- prioritization of chemicals based on risk assessment;

All data, models, fate and effect assessments, risk assessments, and additional tools and methods developed within the project are operationalized in the CADASTER website www.cadaster.eu. The website provides the user with the opportunity to develop his/her new models and perform risk assessment on chemicals that were not within the domain of CADASTER.