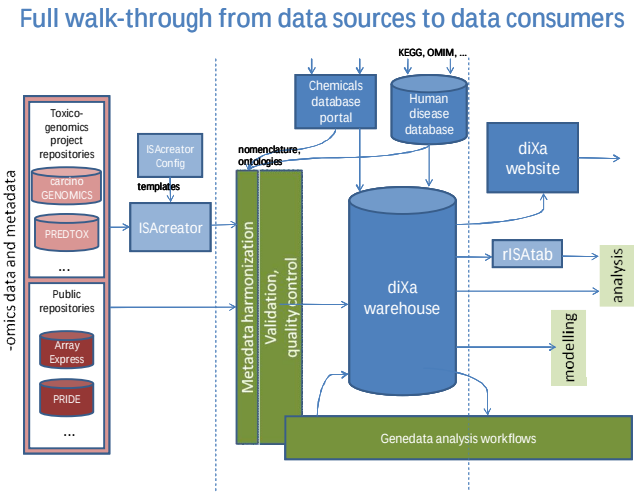
diXa

Summary: The EU nowadays witnesses increasing demands with regard to chemical safety. In particular, animal-based test models need to be replaced preferably by robust, non-animal assays *in vitro/in silico* which better predict human toxicity *in vivo*, are less costly, and are socially better acceptable. For developing such assays, FP6/FP7 Research Programmes are exploiting the revenues of data-dense genomics technologies. However, till date, there is no infrastructure foreseen which aims at capturing all data produced by toxicogenomics (TGX) projects, in a standardized, harmonized and sustainable manner. Data may thus evaporate. The lack of such an infrastructure also prevents innovative breakthroughs from meta-analyses of joint databases and systems modeling. The diXa projects thus responds to the needs the EU Toxicogenomics Research Community, active in exploring cellular technologies and data-dense 'omics technologies in combination with advanced bioinformatics and biostatistics, for the purpose of developing non-animal tests for chemical safety, for a robust and openly accessible data infrastructure for capturing toxicogenomics data and for the deployment of services with regard to data generation, to procedures for harmonization and standardization of toxicogenomics data, as well as to customized tools and techniques for advanced statistics and modeling.

Objectives: The general objective of the diXa project is to further develop and adopt a robust and sustainable service infrastructure (e.g. data infrastructure and e-science environment) for harbouring multiplexed data sets as produced by past, current and future EU research projects on developing non-animal tests for predicting chemical safety, in linkage with other globally available chemical/toxicological data bases and data bases on molecular data of human disease. The feasibility of this approach for developing in silico 'omics-based alternatives for current animal models for evaluating chemical safety will be demonstrated.



Action plan: Workpackage 3 *Data warehousing* relates to retrieving all raw and processed data with their contextual information (sample characteristics, technologies used, type of measurements, etc) from relevant EU Toxicogenomics projects, to capture and to centrally store these data in a standardized and sustainable data warehouse, and to cross-check these data for quality and for initial data processing. Workpackage 4 *Chemicals data base portal* will create a common portal for accessing globally existing chemical/toxicological data bases, deemed relevant and of sufficient quality to be linked to the diXa data infrastructure. Workpackage 5 *Human Diseases Data Base* will create a common portal for accessing globally existing data bases holding molecular signatures of human diseases, thus allowing for the ultimate meta-analyses which connect 'omics responses to exposure to chemicals (Workpackage 3), with their known toxic features (Workpackage 4), to molecular data on human disease status. Workpackage 6 *Cross-check of quality control and initial data analysis* will cross-check the quality of raw and processed 'omics data for quality control and data normalization procedures. Workpackage 7 *User and application support services* will address the support services necessary to ensure interoperability and a seamless data sharing between de diXa data infrastructure and participating EU Toxicogenomics projects, which is key for achieving diXa's objectives. Where the Joint Research Activity of the diXa project will demonstrate the feasibility of the diXa approach for developing non-animal based, *in silico* predictors of human toxicity,

continued overleaf

Project acronym:
diXa

Contract n°: RI-283775

Project type: CP-CSA

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Duration: 36 months

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3.678.746 €

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2.800.000 €

Total funded effort in person-month:
326,63 PM

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Project participants:

UM	NL
EMBL	UK
MPG	D
GD	CH
IMPERIAL	UK
JRC	BE
UKK	D

Keywords:
toxicogenomics, chemical safety, data infrastructure

Collaboration with other EC funded projects:
Carcinogenomics
Predtox
Predictomics
PREDICT-IV
DETECTIVE
Sens-it-iv
ESNATS

Data Infrastructure for Chemical Safety - RI 283775

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Workpackage 8 *Integrative data analysis* will perform an integrative data analysis at various levels of complexity exploiting data from different studies, different cellular models and different analytical platforms. Workpackage 9 *Computational modelling* will deploy these molecular pathways of liver toxicity to develop automated and validated computational models for repeated dose liver toxicity. Workpackage 1 *Management* relates to the management of the diXa project while Workpackage 2 *Training Dissemination* will organize effective training of young scientists, especially in the area of bioinformatics and biostatistics.

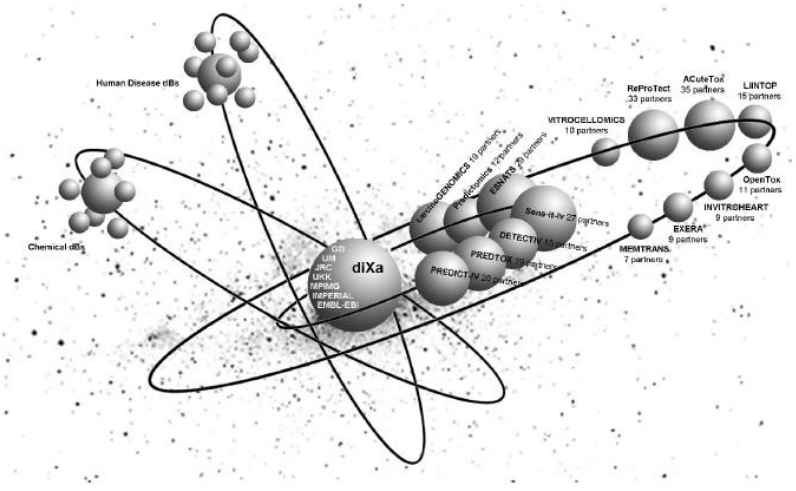
***Networking activities*:** Driven by the needs of the TGX research community, diXa will focus on networking activities, for building a web-based, openly accessible and sustainable e-infrastructure for capturing TGX data, and for linking this to available data bases holding chemico/physico/toxicological information, and to data bases on molecular medicine, thus crossing traditional borders between scientific disciplines and reaching out to other research communities.

***Service activities*:** To advance data sharing, diXa will ensure clear communication channels with and deliver commonly agreed core service support to the TGX research community, by providing SOPs for seamless data sharing, and by offering quality assessments and newly developed tools and techniques for data management, all supported by hands-on training.

***Joint Research activities*:** Through its joint research initiative, by using data available from its data infrastructure, diXa will demonstrate the feasibility of its approach by performing cross-platform integrative statistical analyses, and cross-study meta-analyses, to create a systems model for predicting chemical-induced liver injury.

User communities: The dissemination strategy of diXa is integrated and synergistic with those of the other collaborating EU FP6/FP7 projects, that there is effective engagement with appropriate industry groups form pharma, cosmetics and chemical industry, and the regulatory agencies and that dissemination and training is sustained beyond the formal time frame of the project. In this respect, important stakeholders to address are the EU's regulatory authorities such as the Scientific Committee on Consumer Safety (SCCS), the European Chemical Agency, (ECHA), the European Medicines Agency (EMA) and the European Food Safety Authority (EFSA). Additionally, relevant industrial trade organizations such as COLIPA, CEFIC, EFPIA and ILSI as well as their individual members will be targeted.

International aspects: It is appreciated that the development of a European approach with regard to research infrastructures, including computing and communication based e-infrastructures, and the carrying out of activities in this area at a European level, can make a significant contribution to boosting European research potential and its exploitation, as well as to reinforcing European research communities. The diXa project will thus create the proper scientific e-infrastructure for researchers in the domain of finding alternatives to current animal-based test models for chemical safety to obtain new insights as highly desired because of EU policy demands. Because of its open accessibility, researchers from different scientific disciplines from Europe and beyond, can collaborate on the same data set.



e-infrastructure