Integrating Predictive Toxicology Applications & Resources

An OpenTox Workshop

30 May, 2010

Potsdam, Germany

OpenTox

SEVENTH FRAMEWORK PROGRAMME

Workshop Overview

Barry Hardy

Douglas Connect

OpenTox Project Coordinator

OpenTox

Workshop Overview

1. Introduction & Overview
2. Stakeholder Perspectives
3. Infrastructure Requirements & Interoperability
   - OpenTox Framework Design
4. OpenTox Integrating Application Demonstrations
   - Extensibility, Sustainability & Future Directions
5. Knowledge Café Discussions
   - Concluding Discussion & Actions

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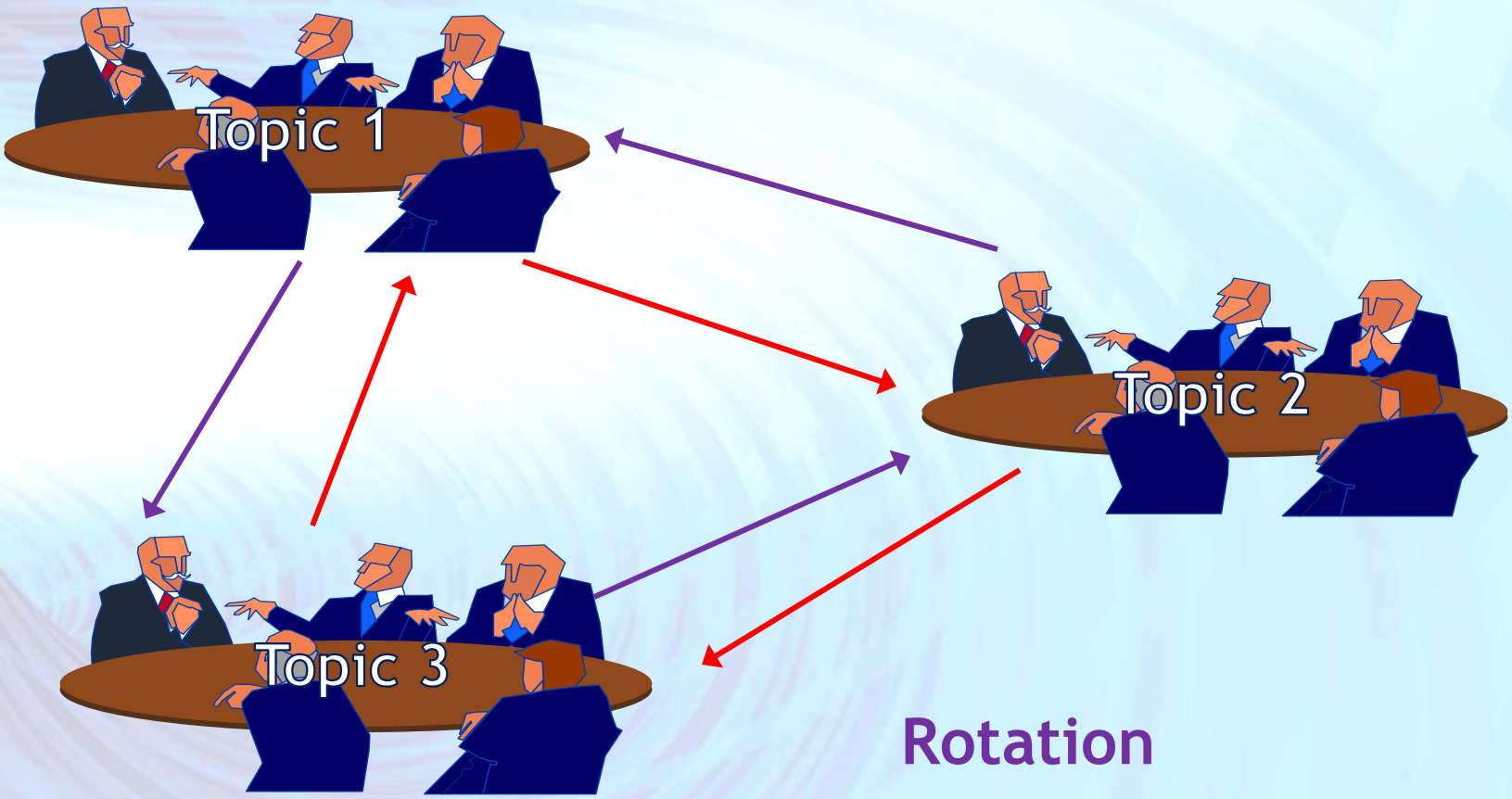
Knowledge Café Discussion Format



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Development of Strategies for Interoperable Resources & Applications in Predictive Toxicology

Eliminate
traditional circus acts, animals

CIRQUE DU SOLEIL

Create
theatrical themes, storylines, new acts

Blue Ocean

Reduce
dangerous acts, traditional humour, transport costs

Raise
tent standards, artistic sophistication, ticket prices!

Based on Blue Ocean Strategy, Kim & Mauborne 2006

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Perspectives

Robert Kavlock (EPA, US)
Carl Westmoreland (Unilever, UK)
Emilio Benfenati (Mario Negri Institute, Italy)
Egon Willighagen (Uppsala University, Sweden)
Jeffrey Wiseman (Pharmatrope, US)
Michael Schwarz (University of Tuebingen, Germany)

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Requirements in Predictive Toxicology Infrastructure

Barry Hardy

Douglas Connect

OpenTox Project Coordinator

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Need for communications in the community overcoming different languages and vocabularies

Explaining the rules of different games on a conservation project trip in the Caprivi, Namibia

From Conservation Project Trip in Caprivi Delta

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SECI Model for Knowledge Management

Tacit

Tacit

Tacit

Knowledge Sharing: Discussions

Socialisation

Externalisation

Explicit

Knowledge Creation from R&D: Data, Codes

Acceptance

Learning: Apply Models

Internalisation

Combination

Knowledege Combination: Predictive Models

Tacit

Explicit

Explicit

Explicit

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Based on Nonaka & Takeuchi, The Knowledge Creating Company, 1995

REACH

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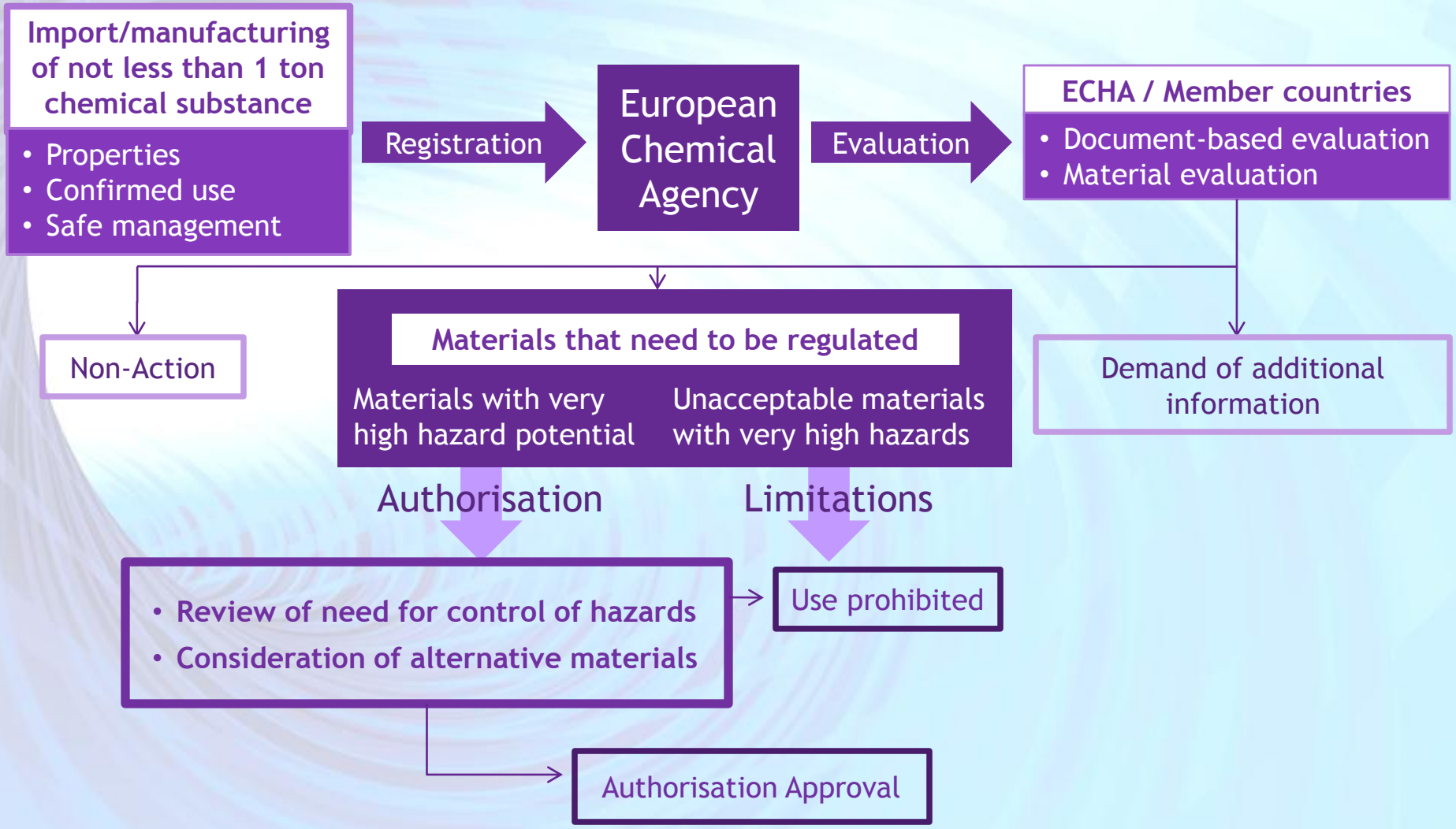
REACH Registration



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What is our situation today when we say ...

Let's build an integrated predictive toxicology application!

Let's collaborate on an analysis!

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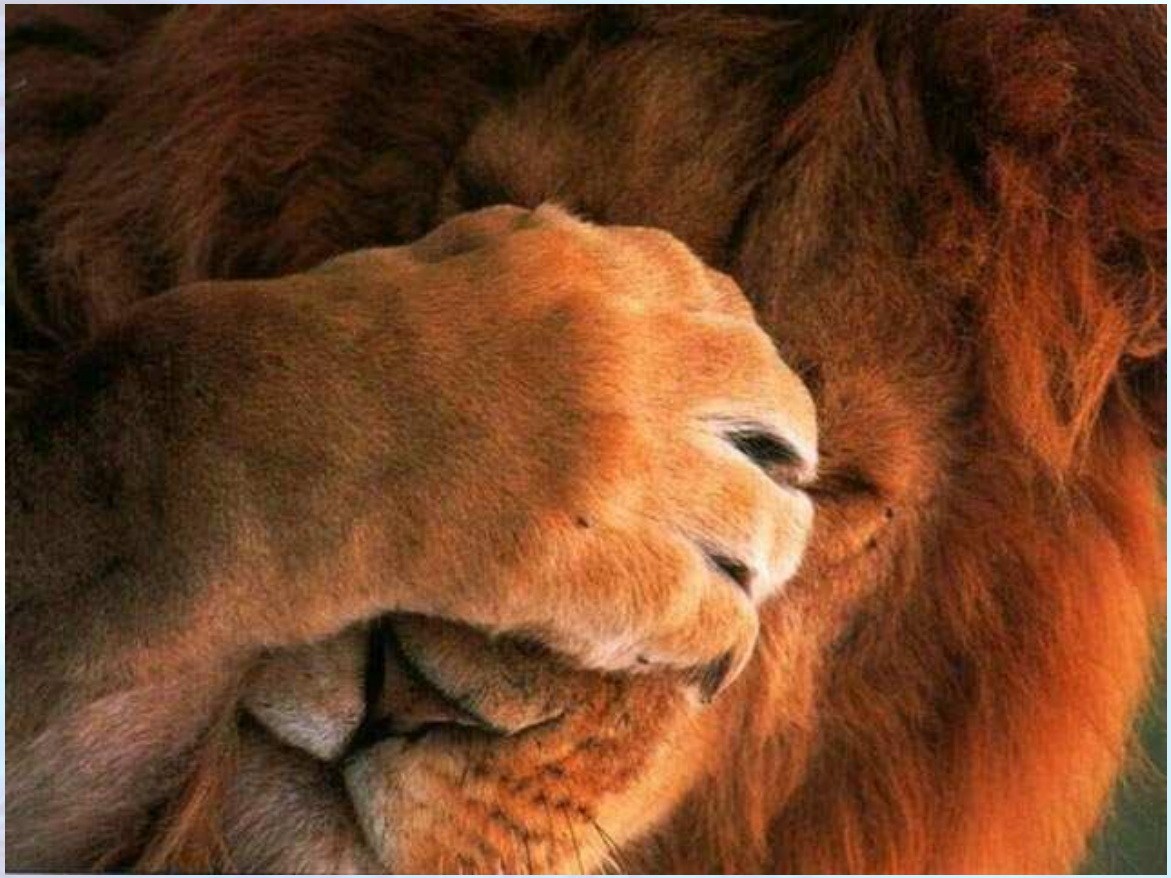
Faced with such an integration challenge ...



... we tend to look away from some of the problems ...

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Faced with such an integration challenge ...

... we tend to look away from some of the problems and from the need to collaborate more closely.

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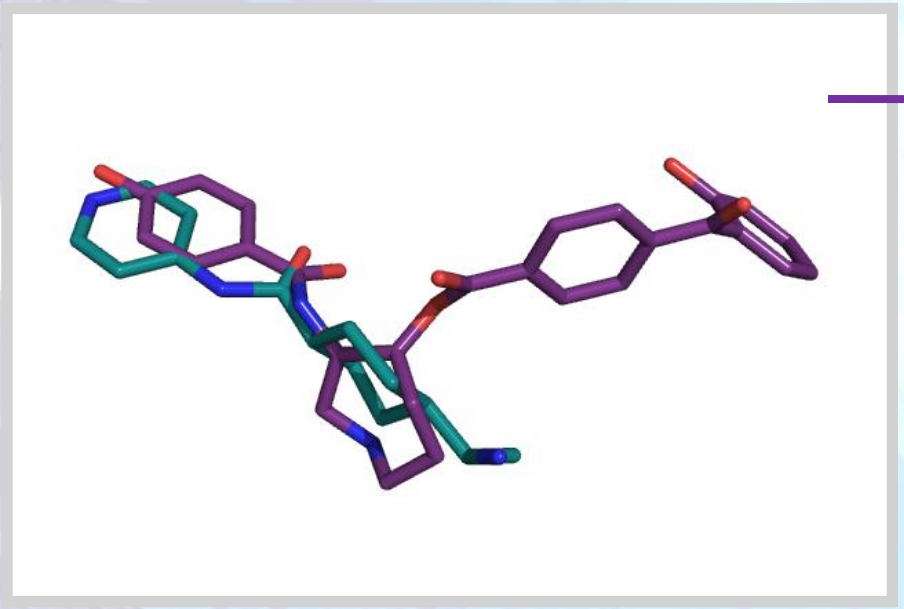
Collaborative Predictive Toxicology Challenge

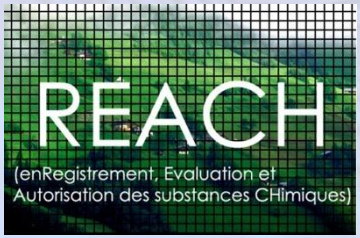
Input Structure



VO

Out – Toxic or Not?

- LD50
- Liver Toxicity
- Secondary Metabolites
- Bioavailability
- Mutagenicity
- Carcogenicity
- ReproductiveToxicology
- Skin Irritation
- Aqua Toxicity
- Combined predictions for arrays of mutiple end points



Driver → Increasing demands on industry to satisfy safety evaluation and risk assessment required by REACH legislation.

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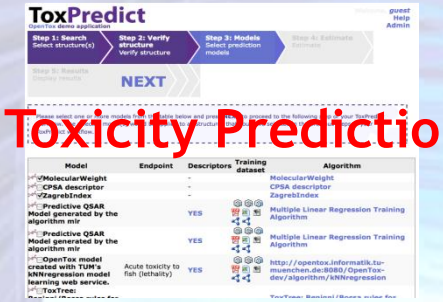
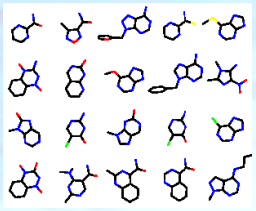
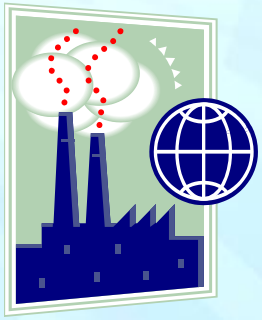
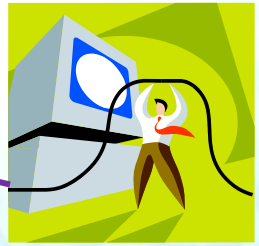
Accelerating Knowledge Flows in Predictive Toxicology

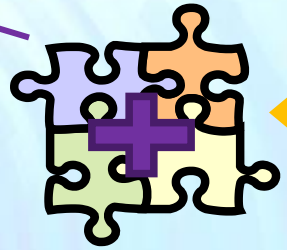


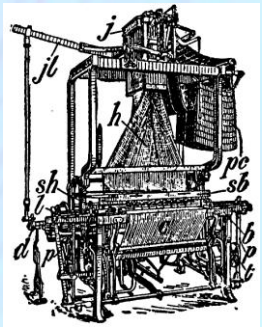
Toxicity Predictions











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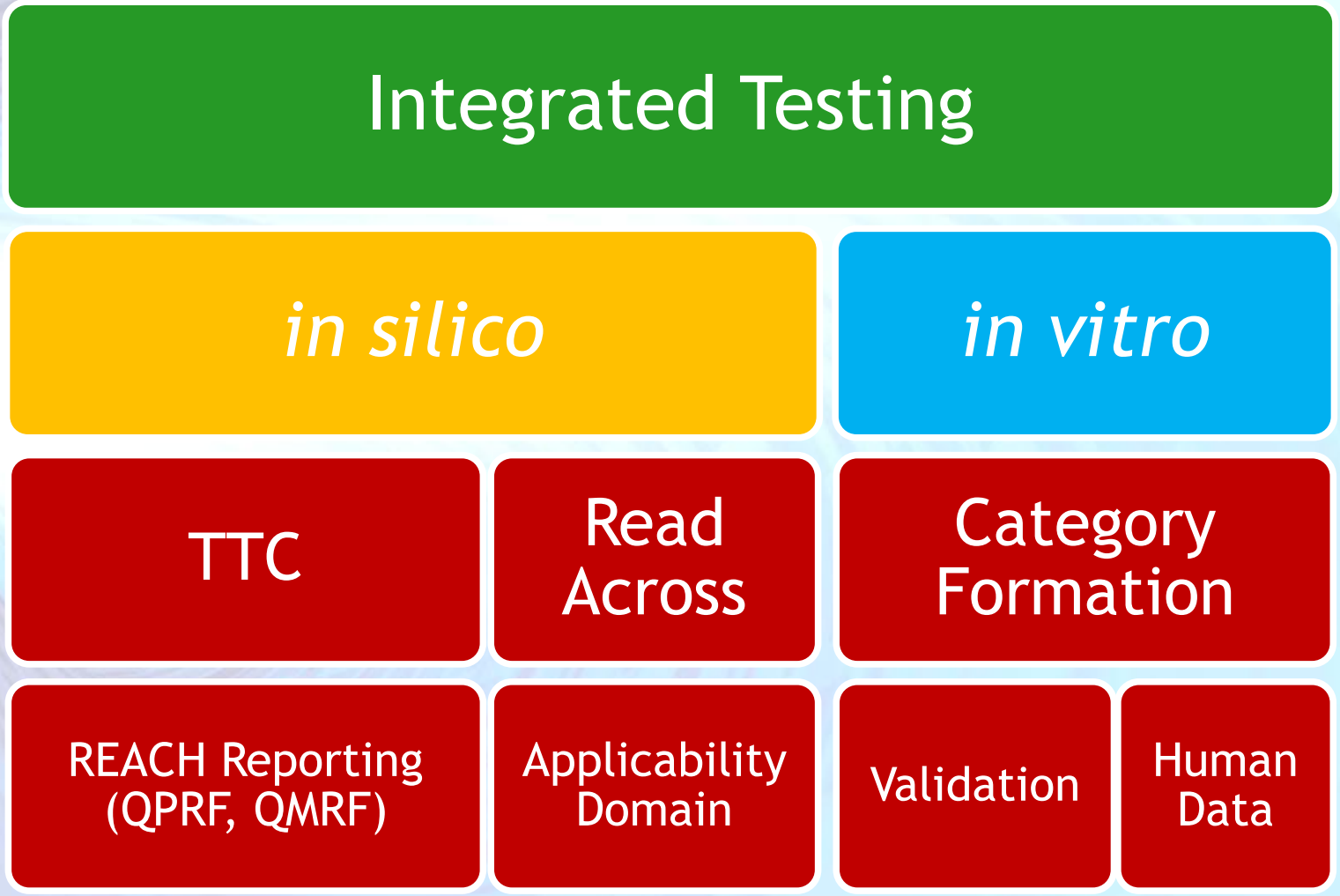
Compelling Needs of Users



Communciated by Grace Patlewicz (Du Pont)

Compelling Needs of Users

Multidisciplinary R&D

Good Support of Flexible Applications

Transparency – Not Black Box!

Mechanistic rationale

QSAR & Expert Systems

Workflows

Automated Integration

Applicability Domain

Categories

Systems Biology

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Communciated by Stephanie Ringeissen (L'Oréal)

Challenges to Integrated Resources & Applications

- Database silos
- Missing information
- Varying quality
- Hard to integrate data
- Hard to integrate models
- No common framework
- Lack of standards
- Lack of validation
- Complex subject
- Application difficult
- Lack of transparency
- Interdisciplinary collaboration

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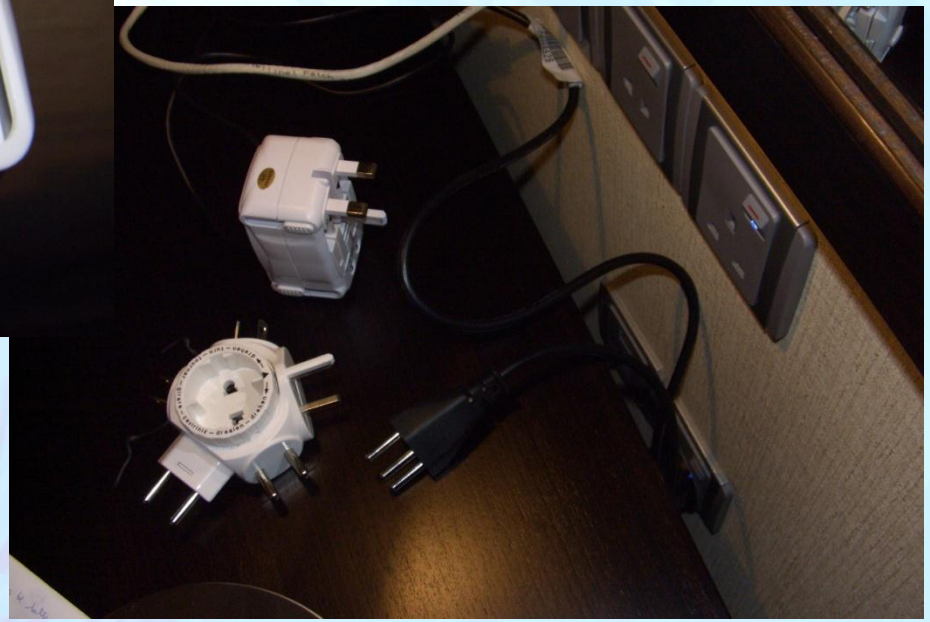
Absence of Interoperability creates Problems



Adaptor Challenge in Jeddah, 2008

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Interacting Components create Solutions

Adaptor Solution in Jeddah, 2008

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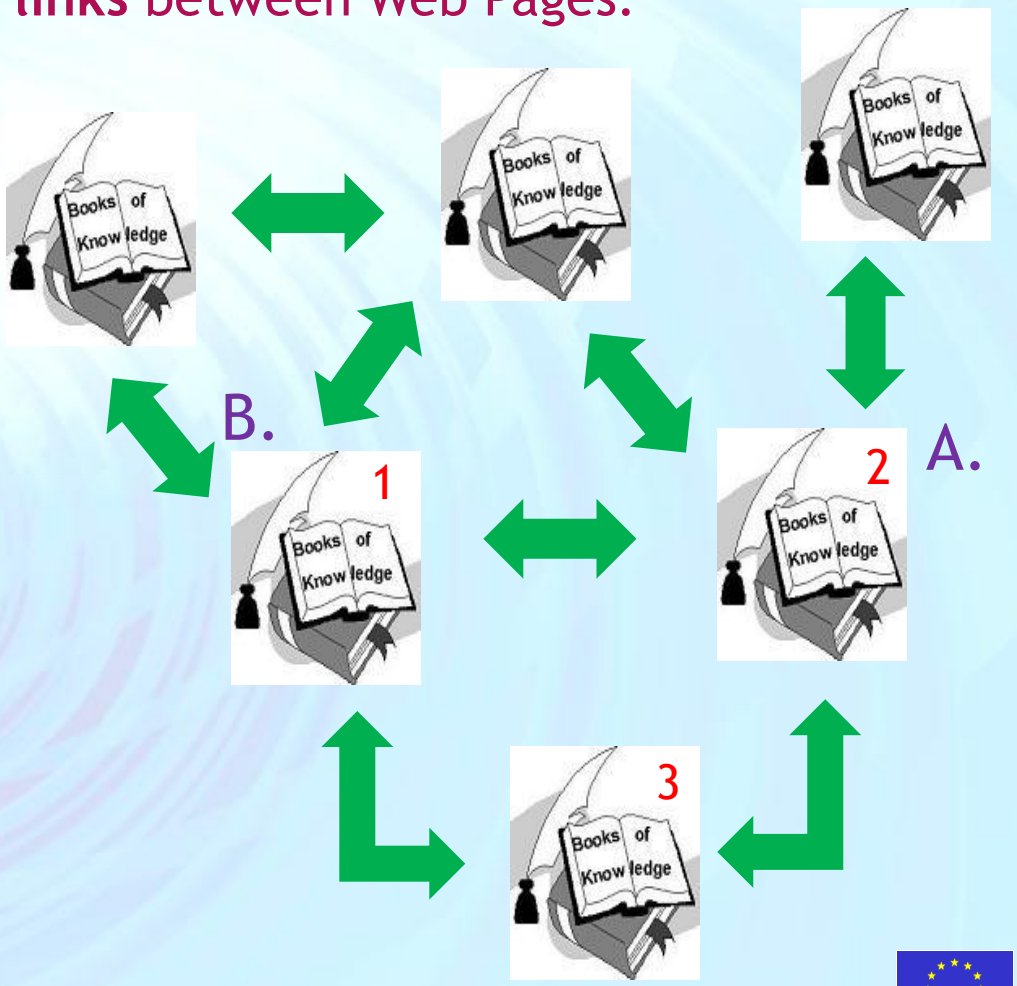
Value is in Linking

The key idea of Google's founders in creating their search engine:
There is useful knowledge in the **links** between Web Pages.

Page Ranking
A page is ranked higher in a search if:

A. it has more connections to it than other pages

B. the pages connecting to it have higher ranking themselves



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Linked Data enables Knowledge Creation, Combination and Analysis

Linked Data is a term used to describe the exposing, sharing, and connecting of data on the Semantic Web using:
URIs a generic means to identify entities in the world
HTTP a simple yet universal mechanism for retrieving resources
RDF a generic graph-based data model with which to structure and link data

Linked Data needs:

1. Provision of a URI that describes a Data Resource
2. Use of HTTP to retrieve useful data from the URI
3. A Data Format described with standardised semantics (so relationships are enabled) e.g. RDF
4. Data should provide links to other Data (through URIs)

Linked Data approach can also be applied to other resource types e.g., for algorithms or models as done in OpenTox…

DBpedia = Linked Data approach applied to Wikipedia

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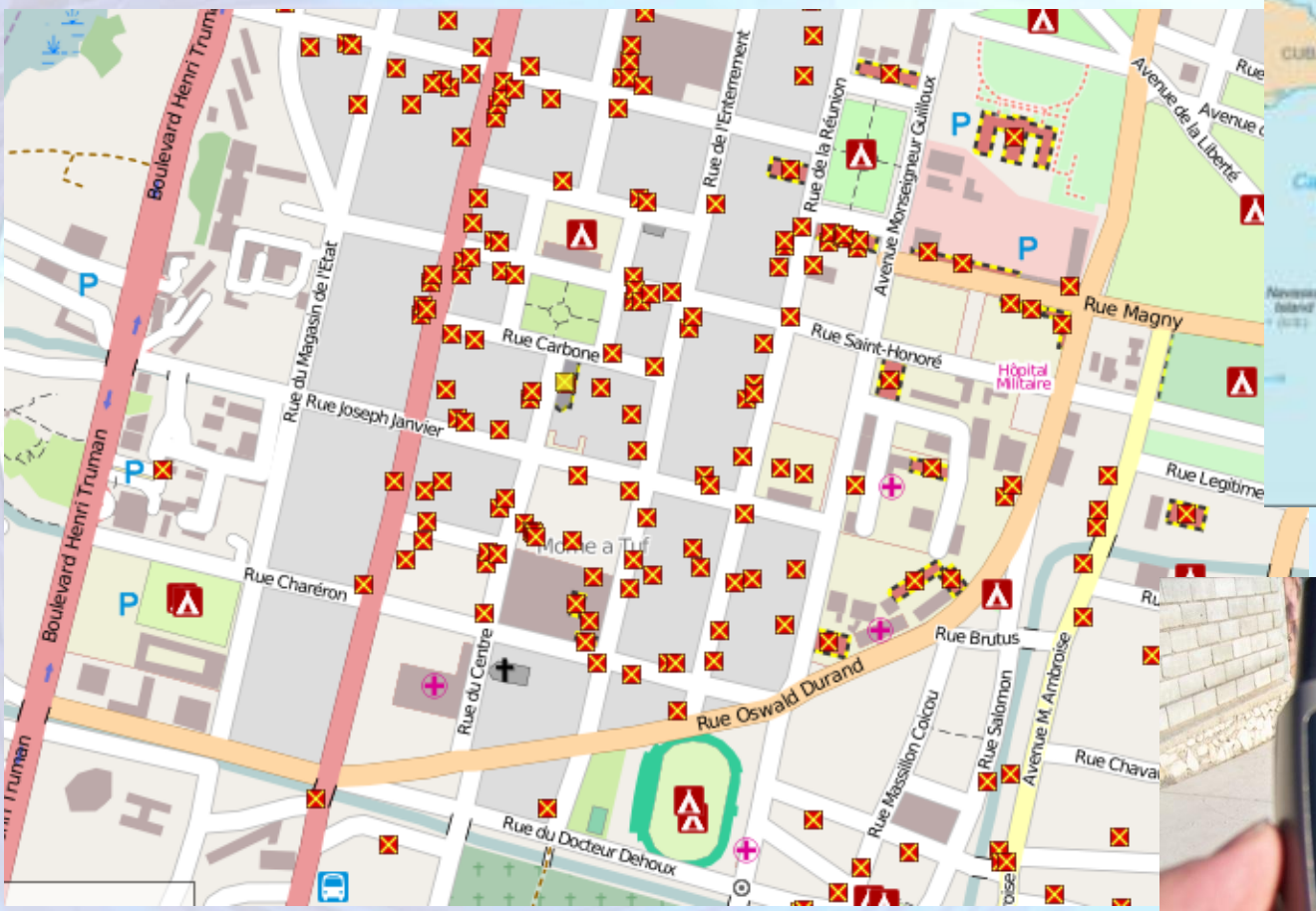
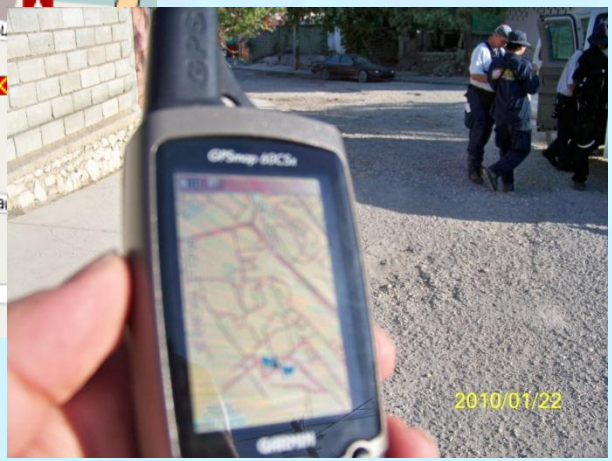
Solution created by Linked Open Data, Web Applications and Crowdsourcing





Haiti Earthquake Crisis Response (2010)

wiki.openstreetmap.org

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Interoperability & Vocabulary

Dogs
- Collie
- Labrador

Cats
- Siamese
- Persian

Birds
- Sparrow
- Owl

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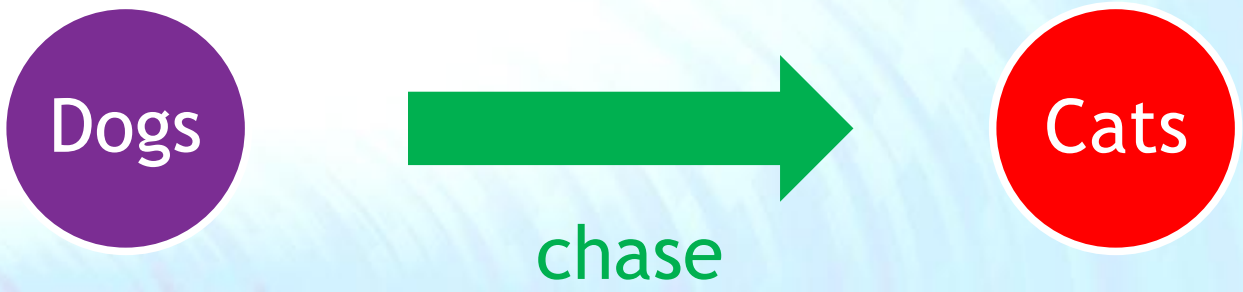
Interoperability & Vocabulary



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Interoperability & Ontology

Org A

Collie

chase

Siamese

Org B

Collie

Siamese

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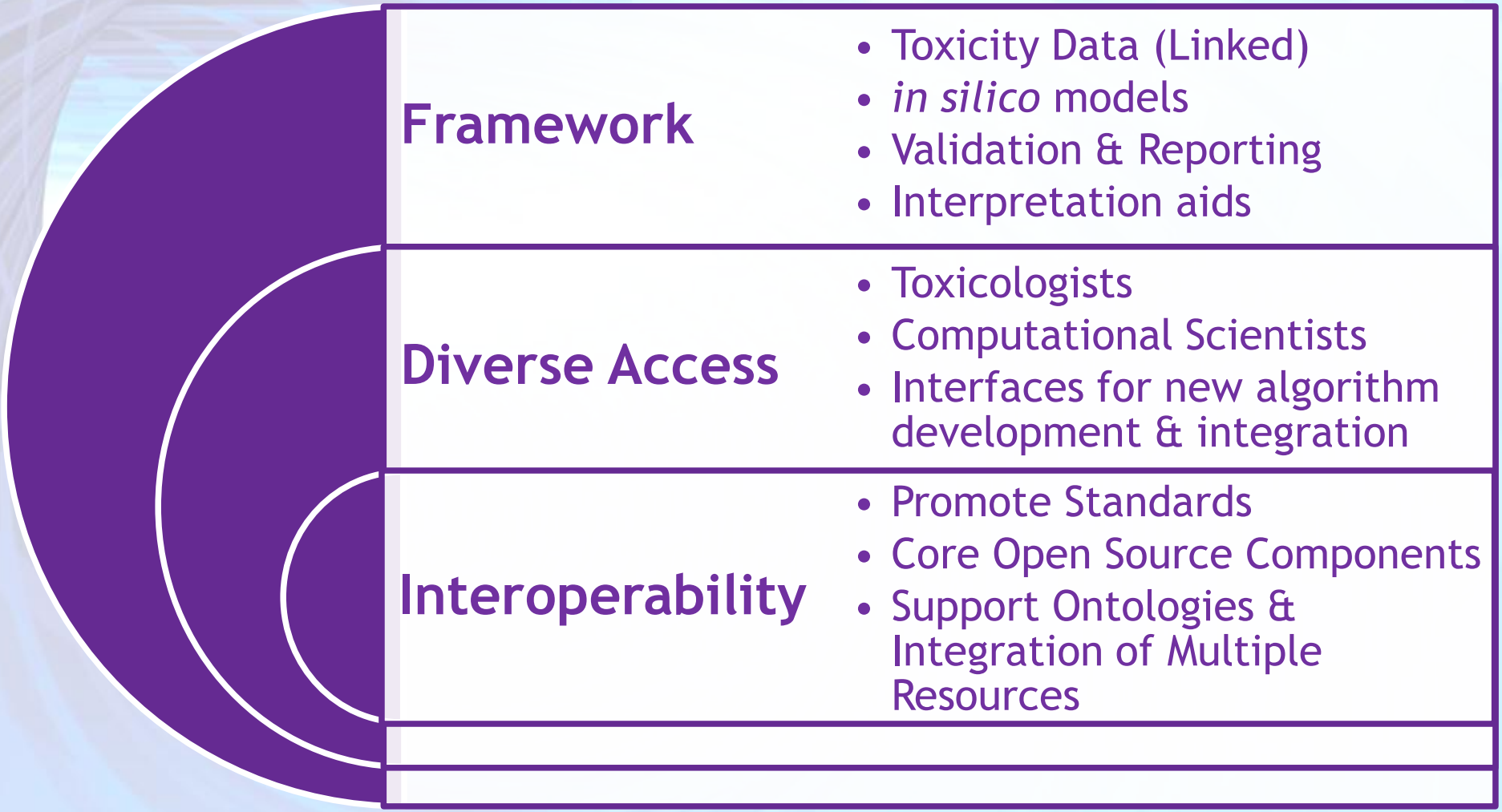
OpenTox Approach



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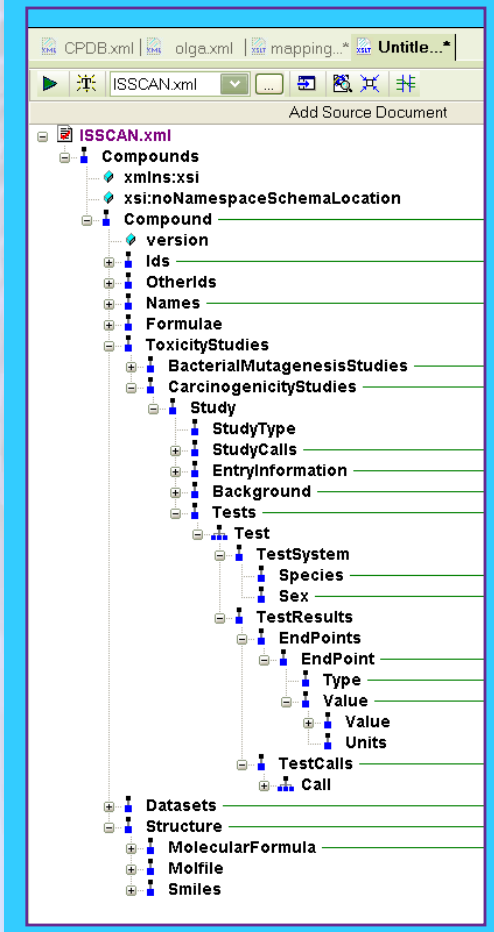
Toxicological Endpoint Ontology Development

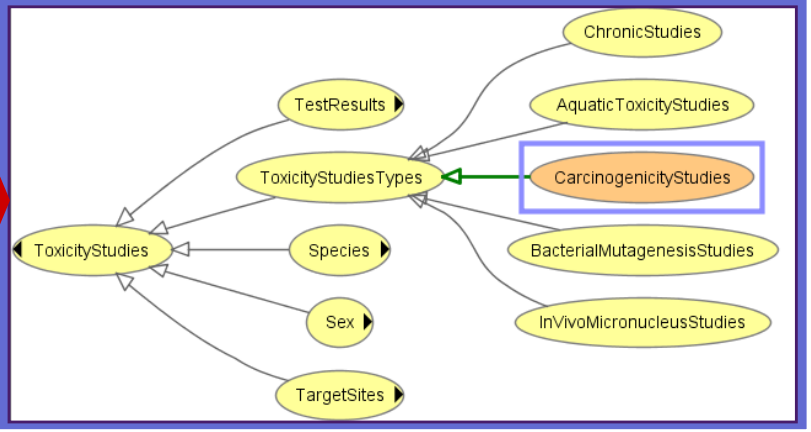
ToxML schema



Other publicly available resources:
DSSTox, GoReni (ITEM), ISSCAN ...

OpenTox Toxicological Endpoint Ontology

Ontology Development



Collaborative Protégé Environment

Re-use of terms defined in neighbouring ontologies (e.g. OBO)

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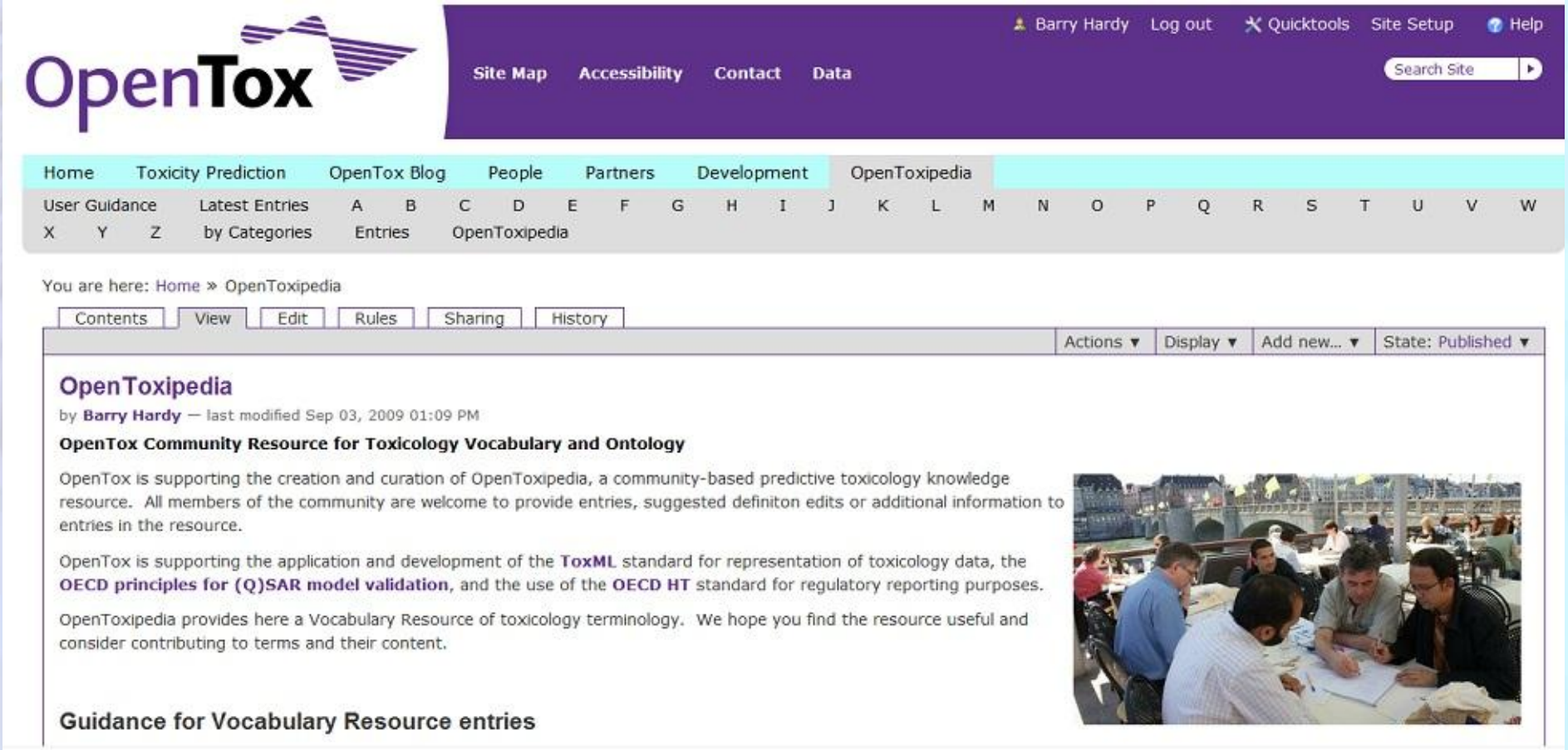
OpenToxipedia



www.opentox.org/opentoxipedia

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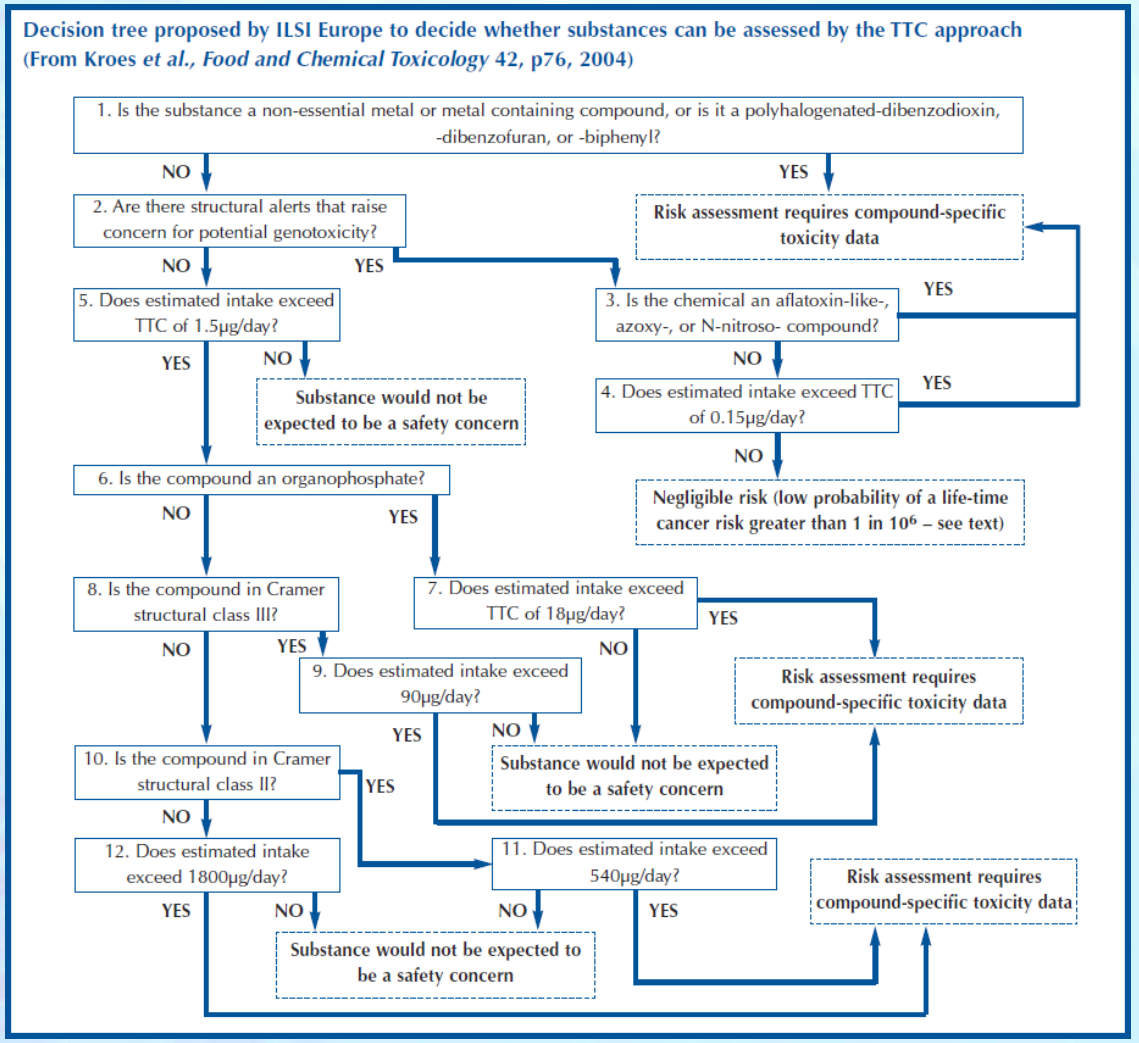
OpenTox Use Case Example

Implement Threshold of Toxicological Concern (TTC) using ILSI decision tree guidelines



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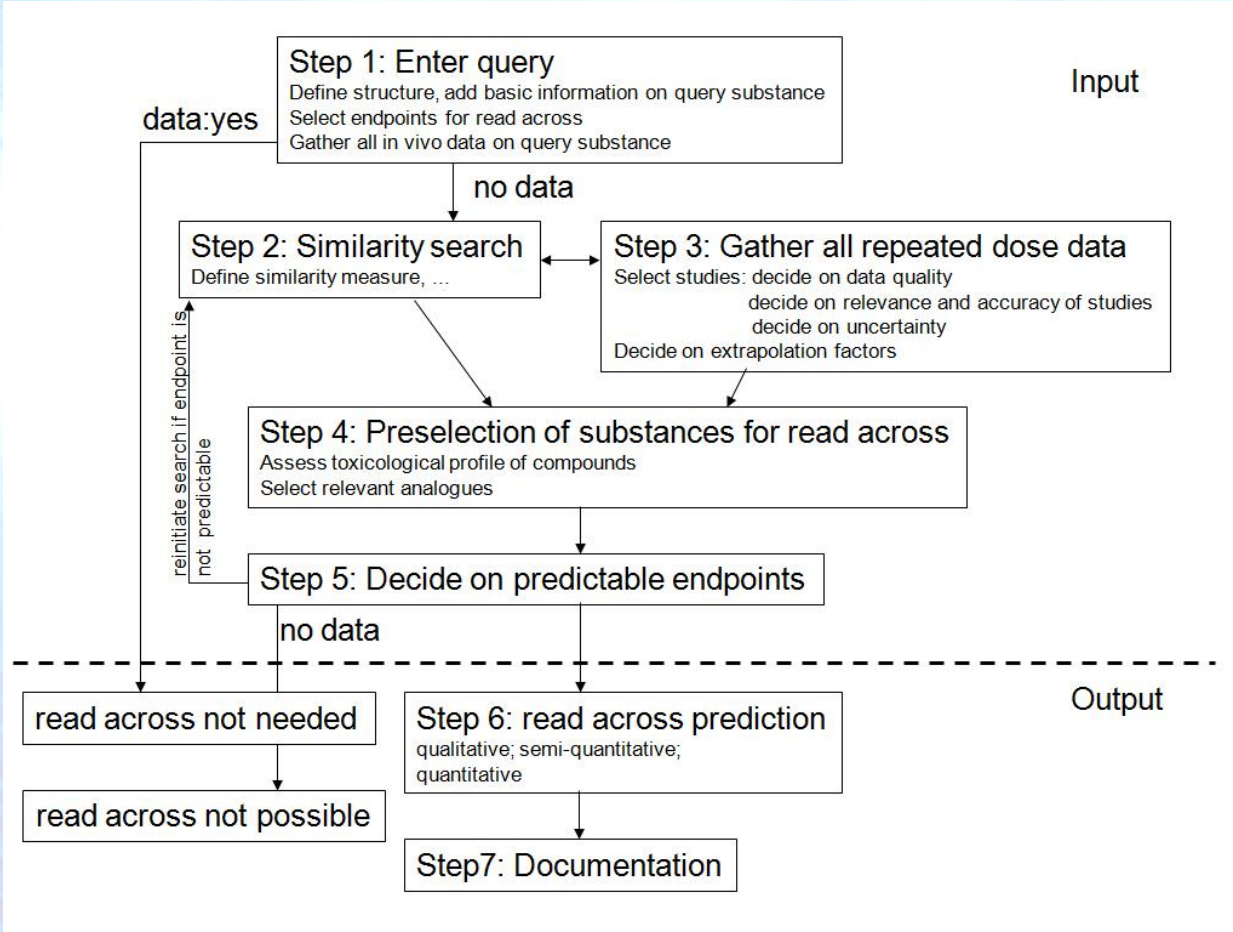
OpenTox Use Case Example

Support Read Across for Repeated Dose Toxicity

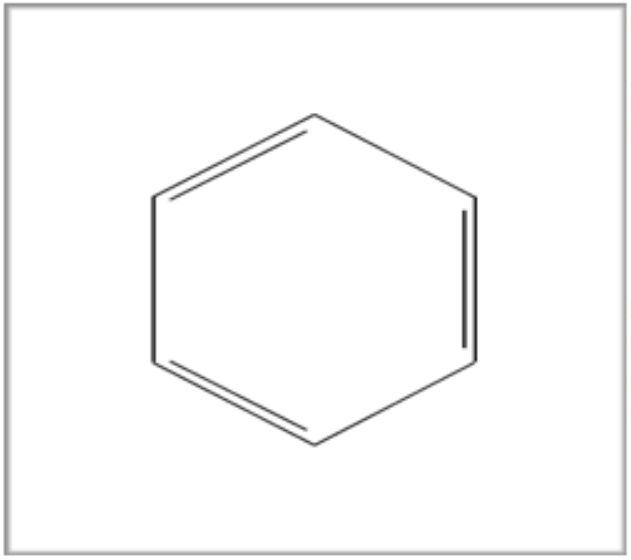


ToxPredict

OpenTox demo application

This page lists your ToxPredict workflow results for the structure(s) you have selected and the model prediction(s) you have chosen to run. You could also retrieve the ToxPredict report in various other formats, e.g. **SDF**, **CML**, **SMI**, **PDF**, **CSV**, **ARFF**, **RDF/XML** or **RDF/N3**.

Download as



CAS RN	71-43-2
EINECS	200-753-7
IUPAC name	benzene
Synonym	(6)annulene; benzine; Benzol; Benzolene; bicarburet of hydrogen; carbon oil; Coal naphtha; cyclohexatriene; mineral naphtha; motor benzol; nitration benzene; Phene; Phenyl hydride; pyrobenzol.
Synonym	21742.0
Synonym	Benzene
Synonym	benzene
Quality label	OK

MolecularWeight MolecularWeight

MW	78.1112

	OECD Principle	OpenTox addresses Validation Principles by...
1	Defined Endpoint	providing a unified source of well defined and documented toxicity data with a common vocabulary
2	Unambiguous Algorithm	providing transparent access to well documented models and algorithms as well as to the source code
3	Defined Applicability Domain	integrating tools for the determination of applicability domains during the validation of prediction models
4	Goodness-of-fit, robustness and predictivity	providing scientifically sound validation routines for the determination of errors and confidences
5	Mechanistic interpretation (if possible)	integrating tools for the prediction of toxicological mechanisms and the recording of opinions and analysis in reports

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The OpenTox Framework Design

Stefan Kramer

Technical University of Munich

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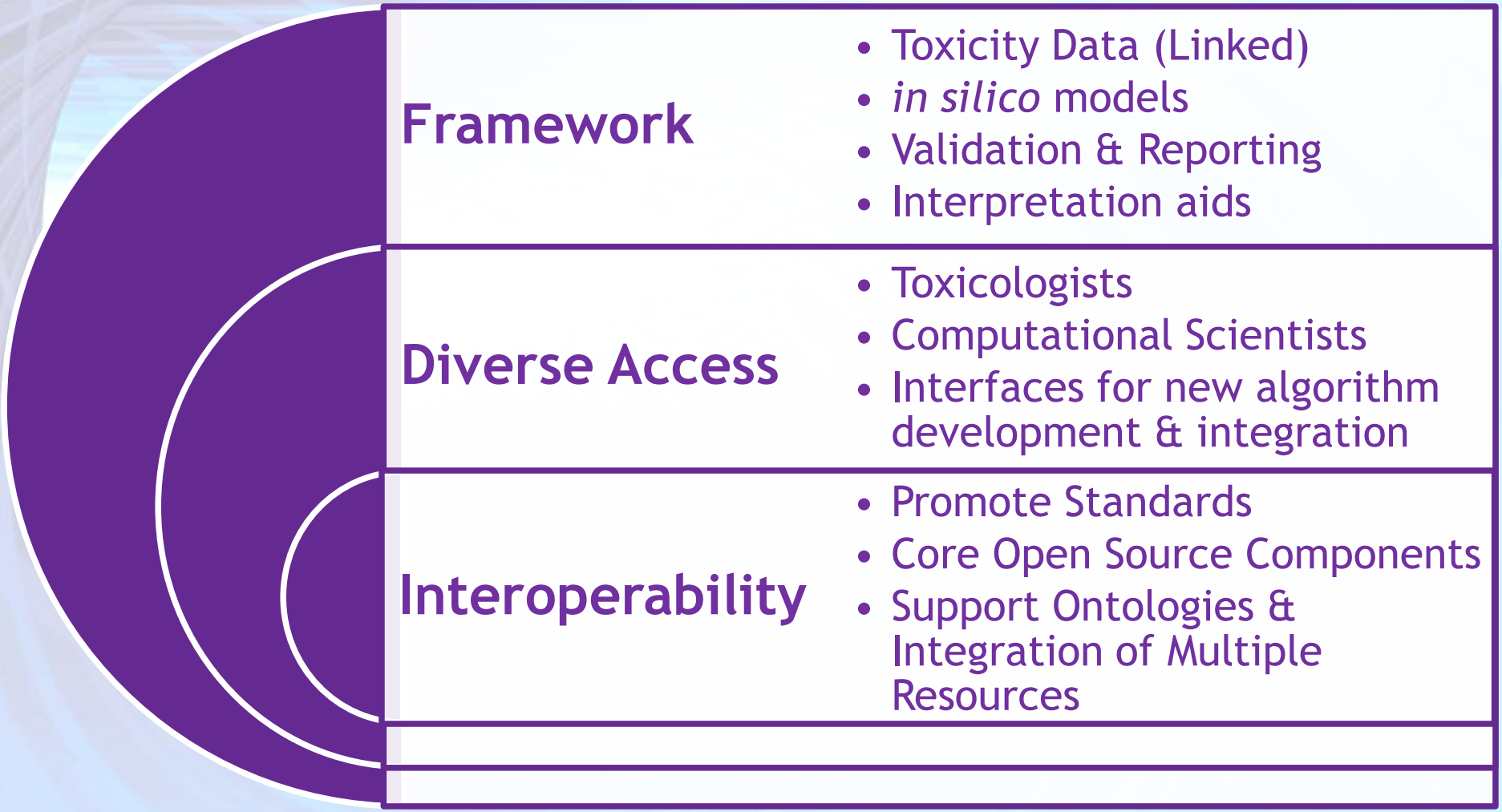
OpenTox Approach



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Strategic Context/Goals

- REACH: possible reduction of test animals by using existing experimental data in conjunction with QSAR
- Also practical needs: **reporting** and form filling
- By the OECD principles,a number of requirements to a framework like OpenTox arise

	OECD Principle	OpenTox addresses by...
1	Defined Endpoint	providing a unified source of well defined and documented toxicity data with a common vocabulary
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Consequences for Requirements on OpenTox

User Requirements		Software Requirements
Umambiguous data	⇒	*formal way of representing information about **data***
Unambiguous access	⇒	*well-defined interfaces*
Transparency of computational tools	⇒	*formal way of representing information about **methods**, well-defined interfaces*
Variety of user groups	⇒	*simplicity and modularity of design*
Need to integrate various resources (e.g., databases, prediction methods, models, …) to make meaningful predictions	⇒	*distributed architecture, interoperability*
Need to integrate biological information	⇒	*again, modularity of design, extensibility*

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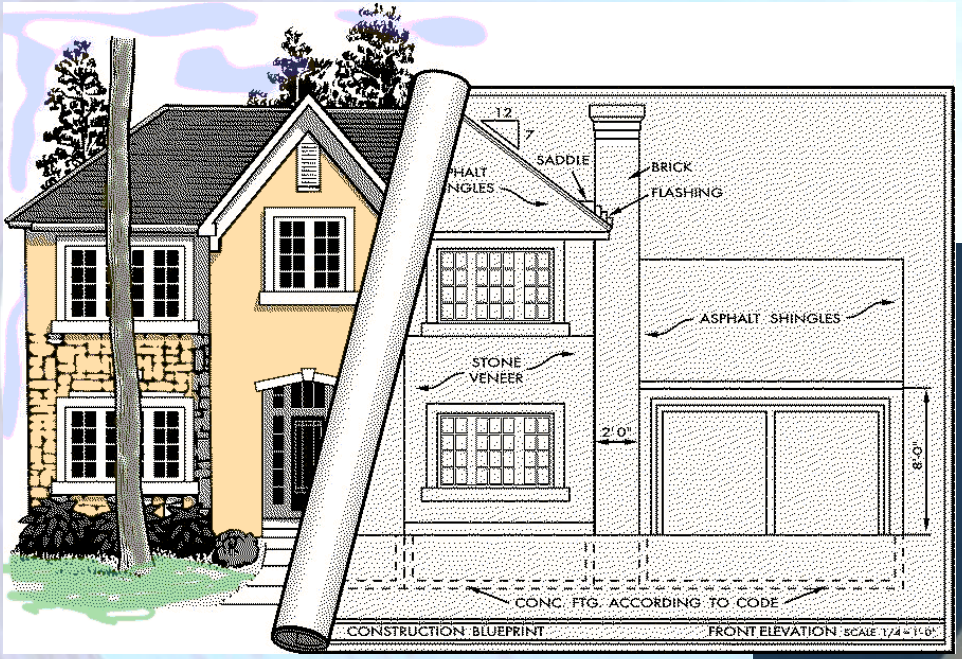
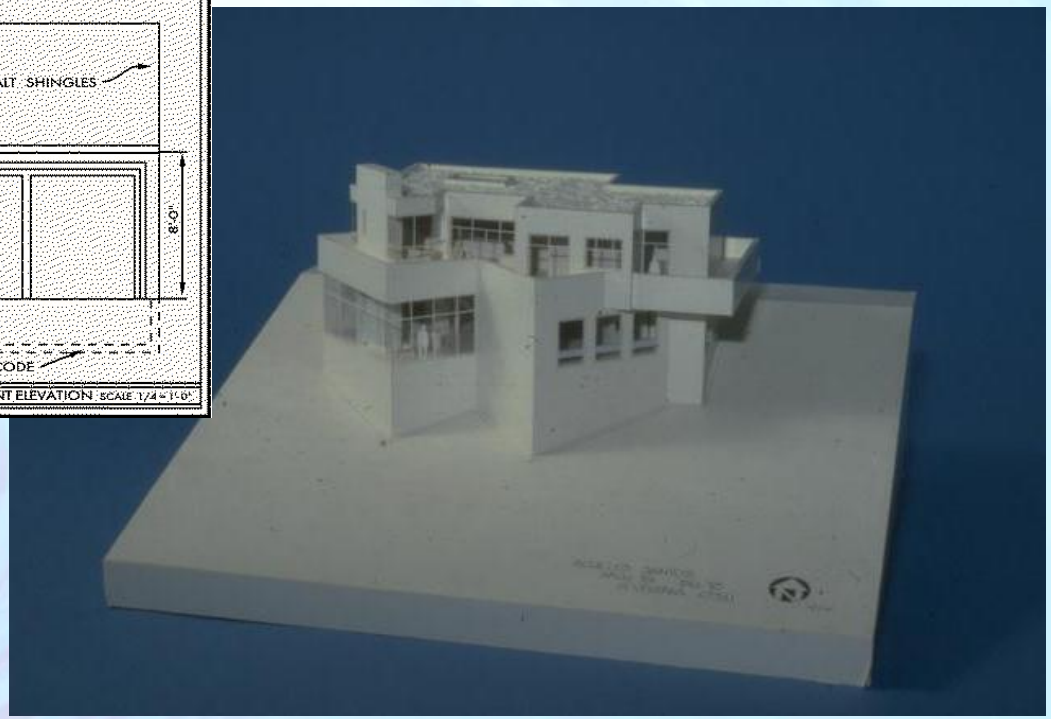
Software Architecture





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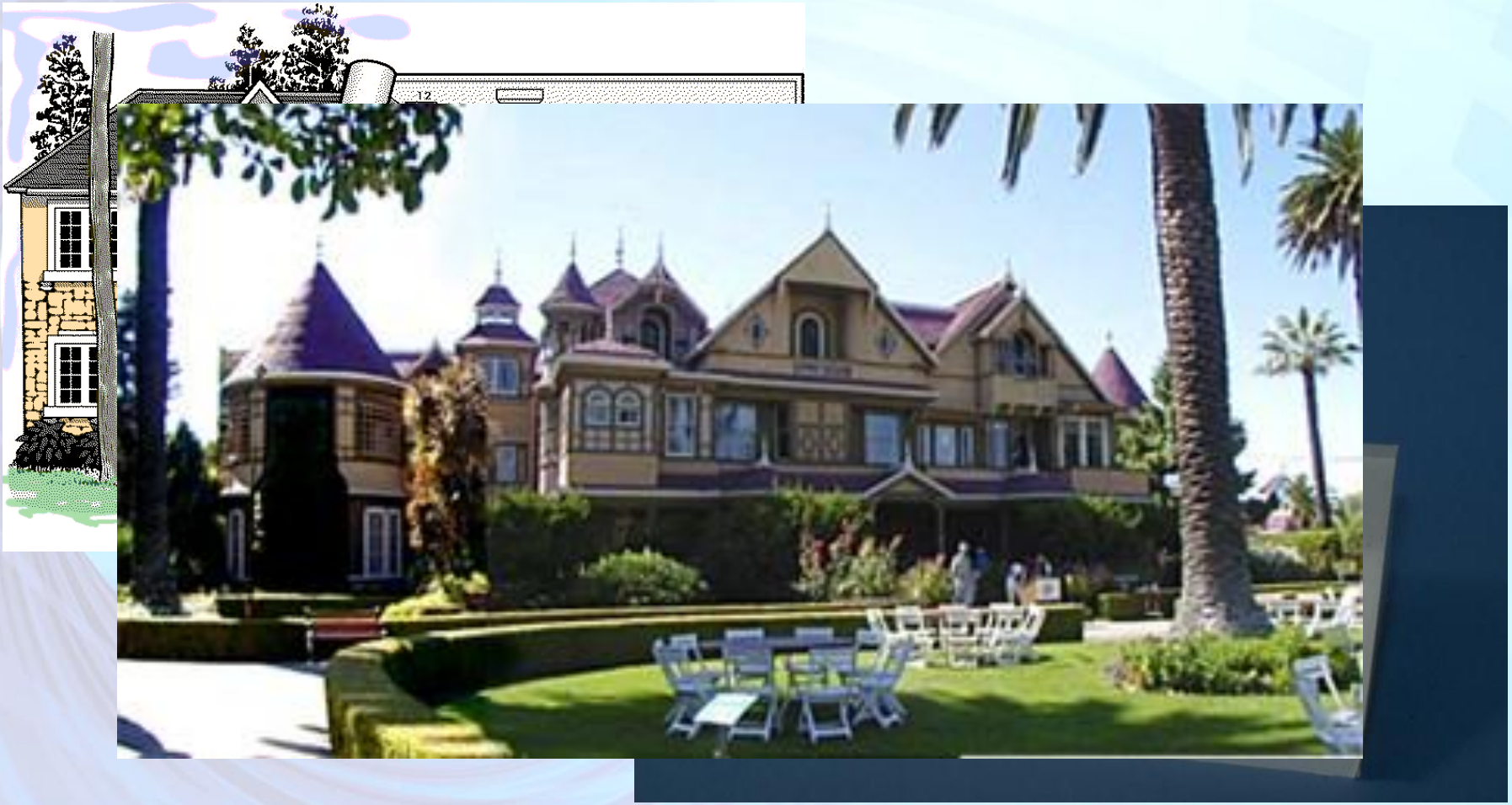
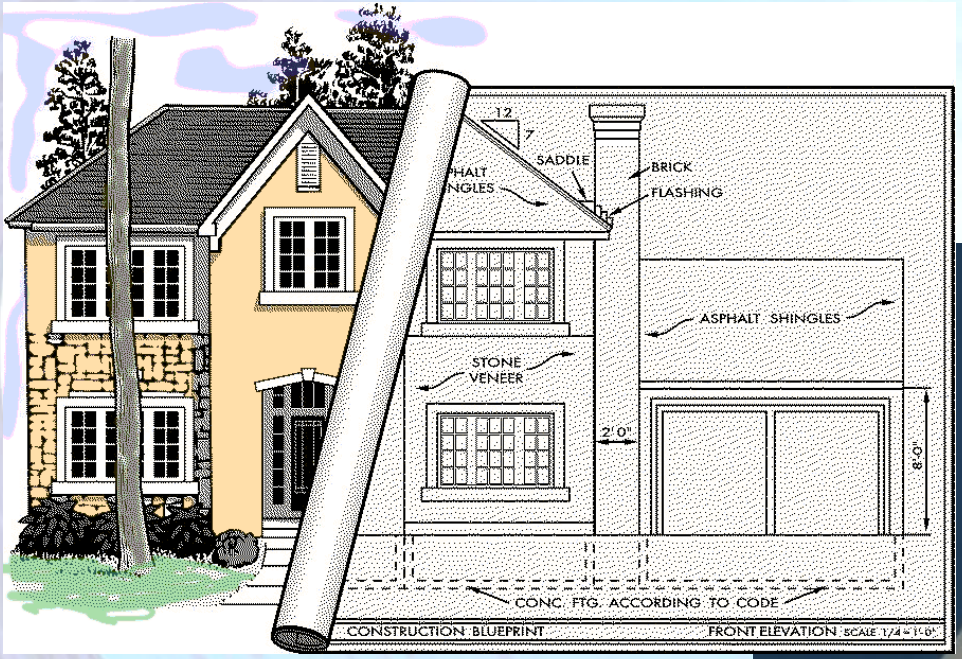
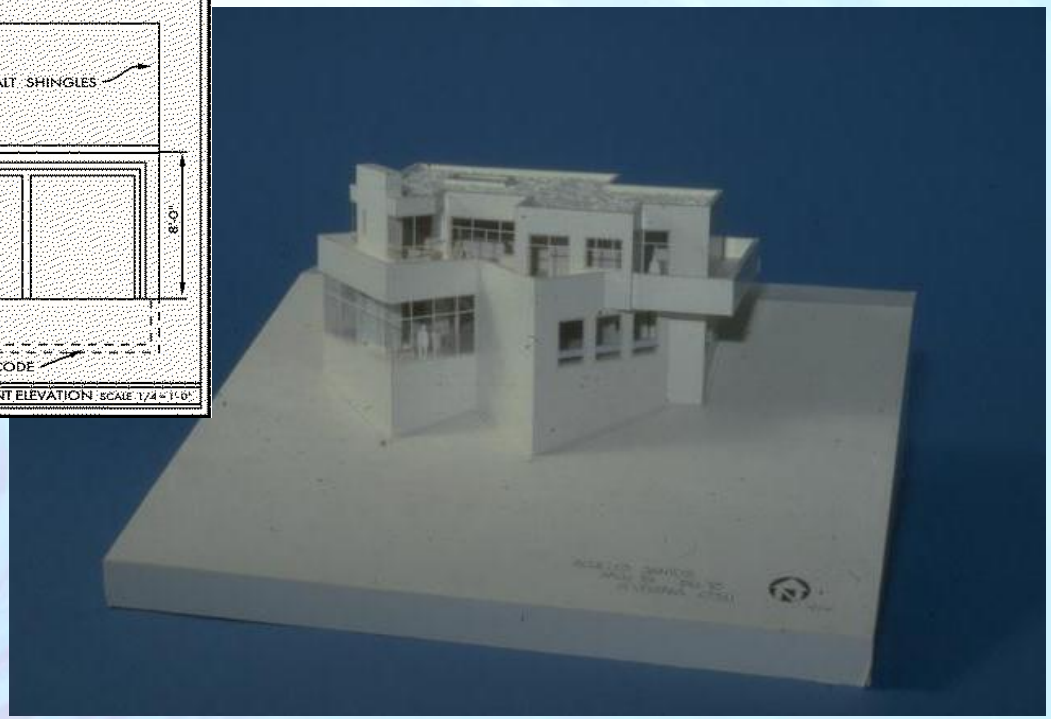
Software Architecture



Software Architecture





To solve a wide range of modelling tasks: needs buildings blocks (modularity) and well-defined ways of combining them

Technological choices…

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Representational State Transfer (REST): What and Why?

What?

- Architectural style for distributed information systems on the Web
- Simple interfaces, data transfer via **hypertext transfer protocol (HTTP)**, stateless client/server protocol
  – GET, POST, PUT, DELETE
- Each **resource** is **addressed** by its own **web address**

Why?

- **Lightweight** approach to **web services**
- **Simplifies/enables** development of **distributed systems**
- (More or less) language independent/installation-free

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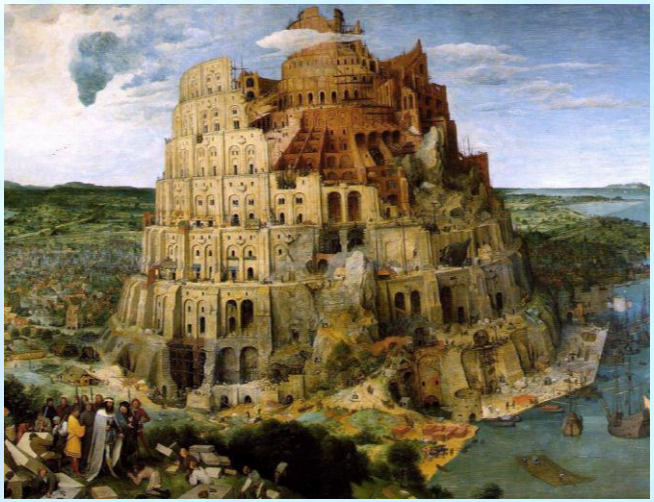
Ontologies: What and Why?

What?

- **Formal**, **shared conceptualization** of a **domain**

Why?

- Distributed services **need** to be able to "talk to each other", i.e. have a **common understanding** of endpoints, any type of property, methods, etc.



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Ontologies

- Standards: **OWL** as representation language and **SPARQL** as query language
- There are many ongoing biological ontology projects
- Our strategy: use existing work and standards wherever possible
- However, there are new ontology needs for OpenTox applications, e.g. for algorithms, toxicological endpoints

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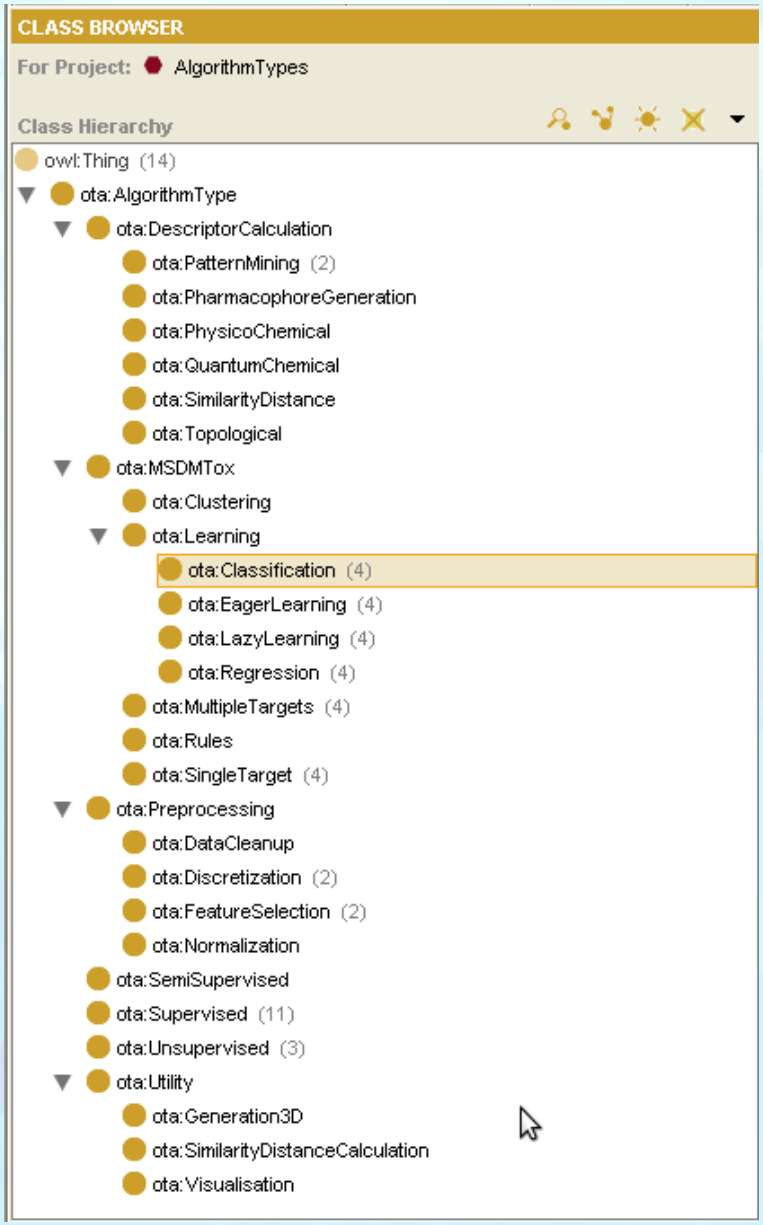
Ontology Working Group



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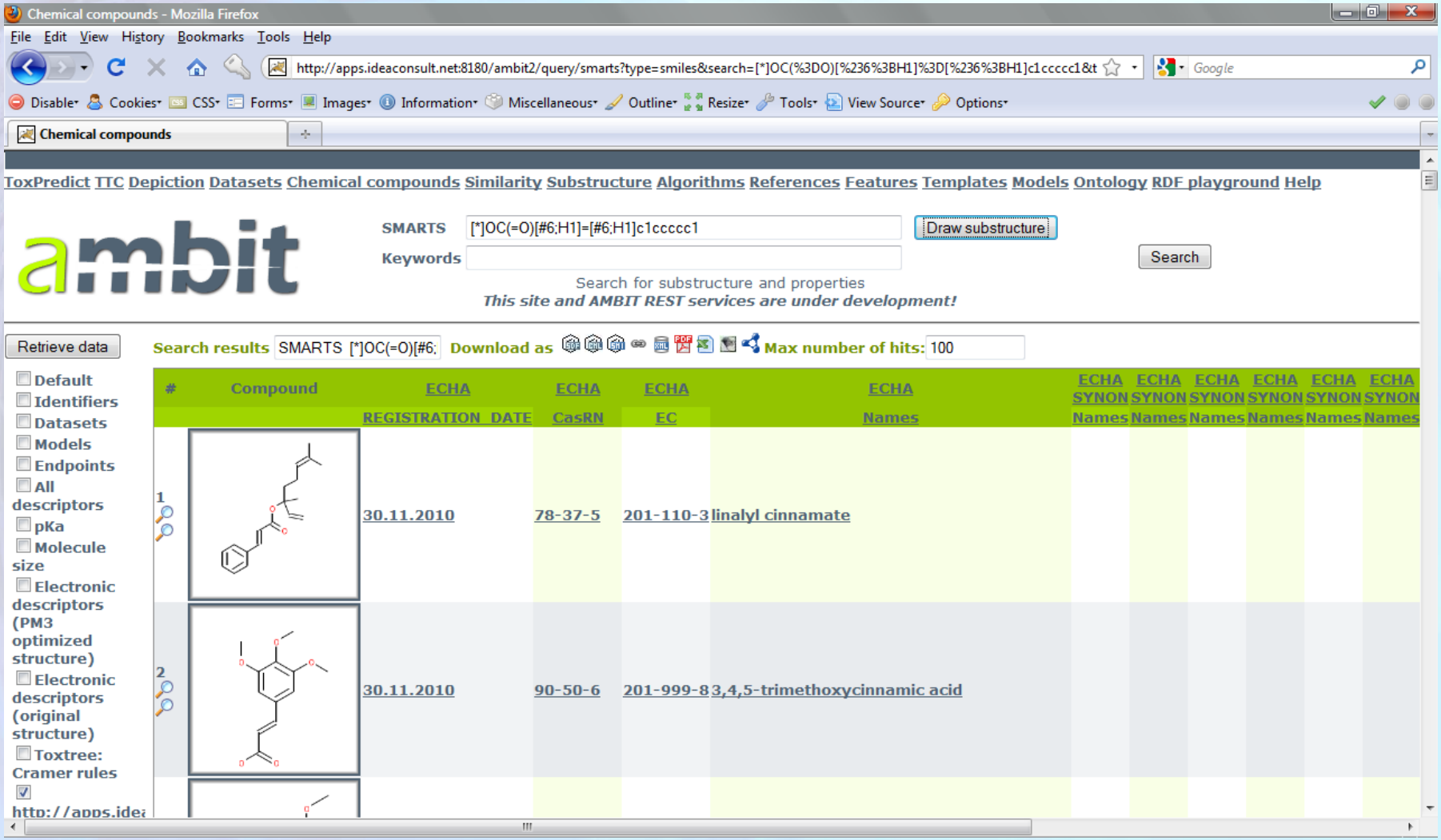
OpenTox: Databases



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OpenTox: Databases

Dataset	OK	Probably OK	Probably ERROR	Unknown	Probably ERROR%
ECHA list of pre-registered substances	N/A	N/A	N/A	N/A	N/A
Chemical Identifier Resolver	67779	5314	3638	3471	4.75%
ChemIDplus	64802	7986	921	1745	1.24%
ChemDraw	17918	1147	502	478	2.57%
JRC PRS list	61332	4833	4022	2880	5.83%
ISSCAN	931	50	98	62	9.40%
CPDBAS	778	37	0	693	0%
DBPCAN	60	2	0	147	0%
EPAFHM	281	5	0	331	0%
KIERBL	102	1	0	175	0%
IRISTR	346	16	0	177	0%
FDAMDD	213	19	1	983	0.08%
ECETOC skin irritation	158	12	0	5	0%
Skin sensitisation (LLNA)	160	7	4	38	1.95%
Bioconcentration factor (BCF) Gold Standard Database	N/A	N/A	N/A	N/A	N/A

Integrating diverse data sources into OpenTox ontology

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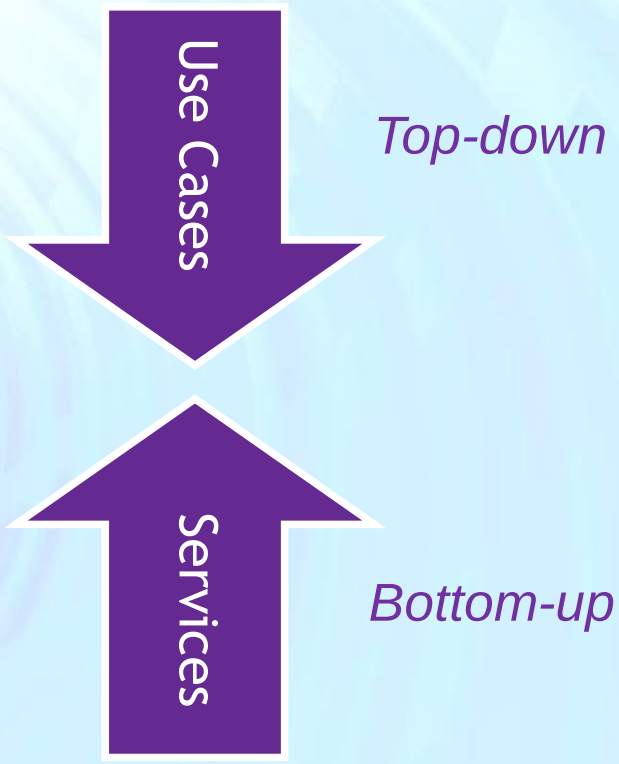
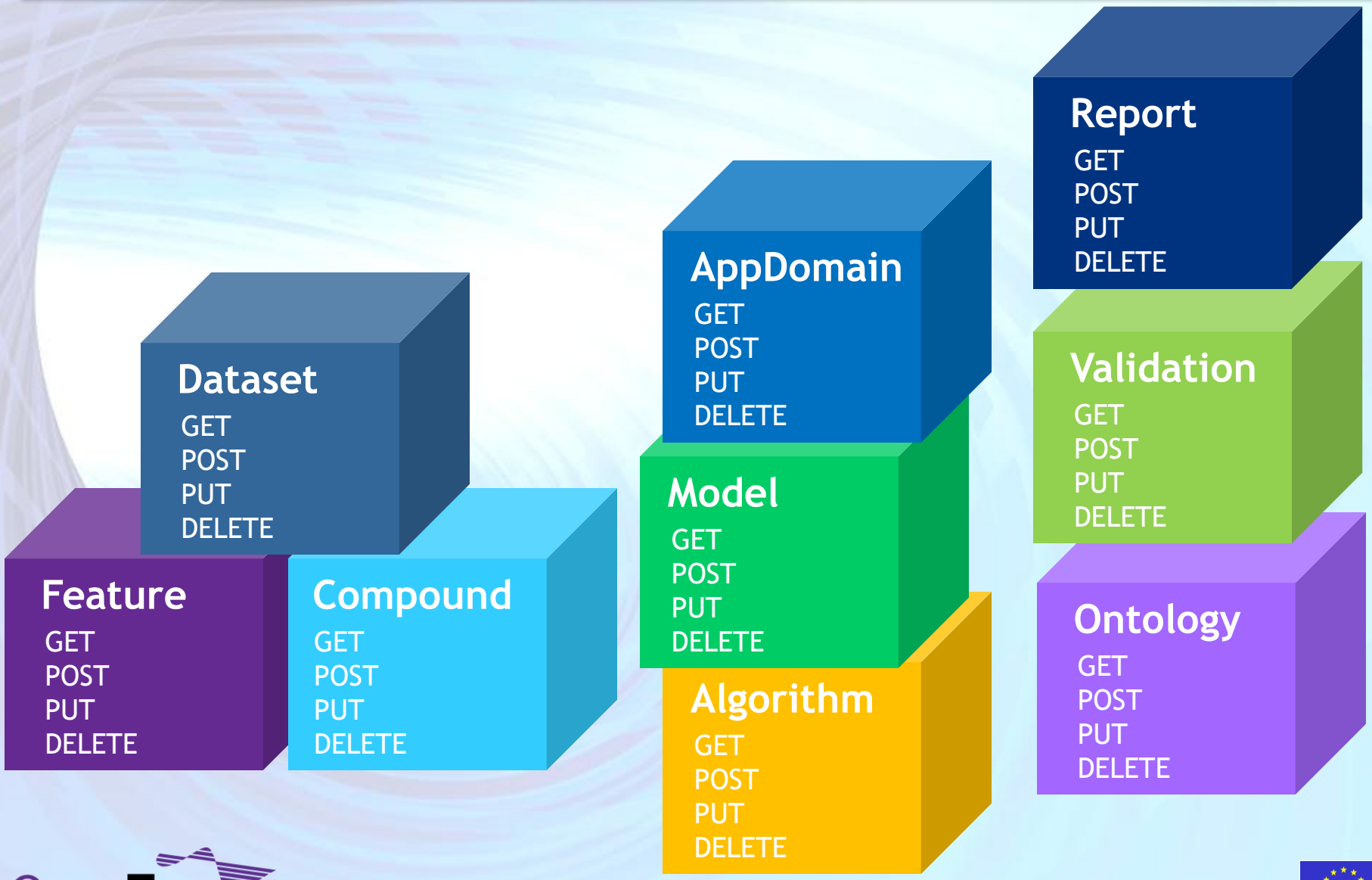
Development Process

- Bidirectional
  - from the services (building blocks) to the use cases, and, vice versa,
  - from the use cases to the services

- Use cases
  - ToxPredict (shown later)
  - ToxCreate (shown later)
  - Read-across
  - ToxCast
  - …



Overview of Application Programming Interfaces



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Interface Definitions

Description	Method	URI	Parameter	Result	Status codes
Get available feature URIs for a compound	GET	/compound/{cid}/feature	?**feature_uris[]**="URIto features" (optional)	Returns representation of the features as uri-list or RDF All available features are returned, if no parameter is specified.	200,404,503
Create a new feature value	POST	/compound/{cid}/feature	?**feature_uri**="URIto feature" (mandatory, single feature)&**value**=the_value	URI of the compound with the new feature, e.g. /compound/{id}?feature_uris[]=the-new-feature	200,400,503
Update a new feature value	PUT	/compound/{cid}/feature	?**feature_uri**="URIto feature" (mandatory, single feature)&**value**=the_value		200,400,404,503
Delete specified features from the compound	DELETE	/compound/{cid}/feature	?**feature_uris[]**="URIto features" (optional)		200,400,404,503

OpenTox

Interface Definitions

Description	Method	URI	Parameters	Result	Status codes
get description of a specific feature definition	GET	/feature/{id}	–	URI-list or RDF representation of a feature.	200,404,503
create a new feature	POST	/feature	**Content-type**="any-of-RDF-types", content=RDF-representation	URI of the new feature definition.	200,400,404,503
update feature	PUT	/feature/{id}	**Content-type**="any-of-RDF-types", content=RDF-representation	–	200,400,404,503
delete feature	DELETE	/feature/{id}	–	–	200,400,404,503
get a list of available feature definitions	GET	/feature	?**query**=URI-of-the-owl:sameAs-entry	URI list or RDF of features found by the query or all available, if query is empty. Returns all features, for which owl:sameAs is given by the query.	200,404,503

OpenTox

Interface Definitions

Description	Method	URI	Parameters	Result	Status codes
Get a list of available datasets	GET	/dataset	Query parameters (optional, to be defined by service providers).	List of URIs or RDF for the metadata only.	200,404,503
Get a dataset	GET	/dataset/{id}	–	Representation of the dataset in a supported MIME type.	200,404,503
Query a dataset	GET	/dataset/{id}	**compound_uris[]** and/or **feature_uris[]** to select compounds and features; further query parameters may be defined by service providers.	Representation of the query result in a supported MIME type.	200,404,503
Get metadata for a dataset	GET	/dataset/{id}/metadata	–	Representation of the dataset metadata in a supported MIME type.	200,404,503
Get a list of all compounds in a dataset	GET	/dataset/{id}/compounds	–	List of compound URIs.	200,404,503
Get a list of all features in a dataset	GET	/dataset/{id}/features	–	RDF or List of feature URIs (pointing to feature definitions/ontologies).	200,404,503

OpenTox

Interface Definitions

Description	Method	URI	Parameters	Result	Status codes
Get a list of all available models	GET	/model	(optional) ?query=URI-of-the-owl:sameAs-entry	List of model URIs or RDF representation. If query specified, returns all models, for which owl:sameAs is given by the query.	200,404,503
Get the representation of a model	GET	/model/{id}	–	Representation of the model in a supported MIME type.	200,404,503
Delete a model	DELETE	/model/{id}	–	–	200,404,503
Apply a model to predict a dataset	POST	/model/{id}	**dataset_uri** **result_dataset**=datasetsuri **dataset_service**=datasetserviceuri	URI of created prediction dataset (predictions are features), task URI for time consuming computations.	200,202,400,404,500,503
Apply a model to predict a compound	POST	/model/{id}	**compound_uri**	Prediction in a supported MIME type; task URI for time consuming computations.	200,202,400,404,500,503

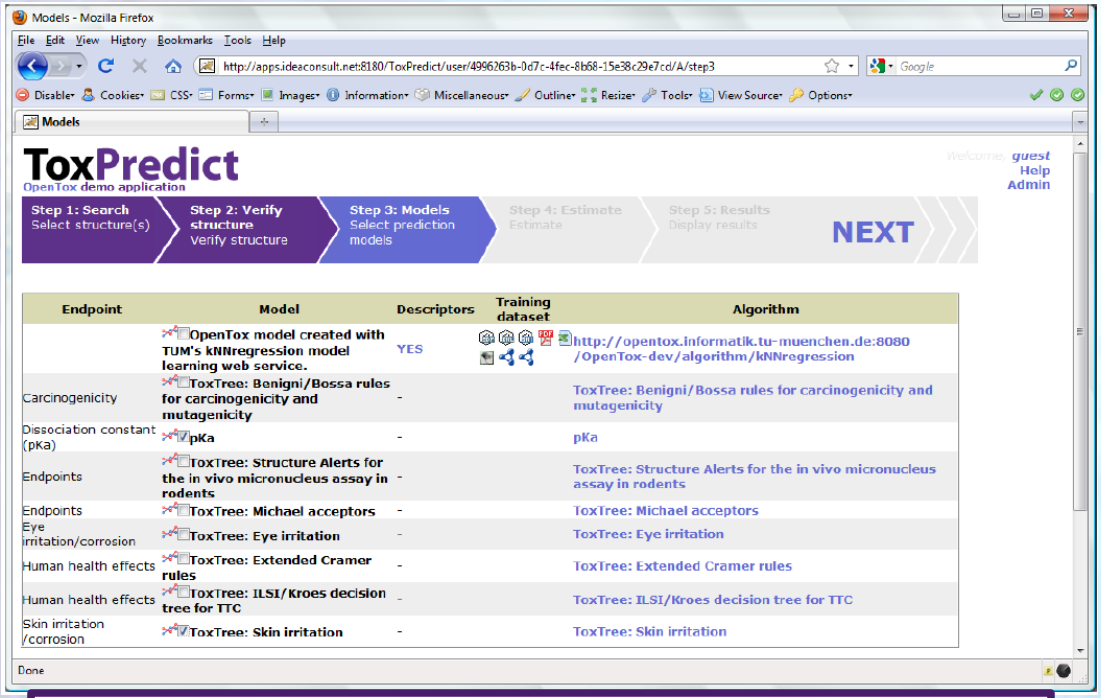
OpenTox

Interface Definitions

Description	Method	URI	Parameters	Result	Status codes
Retrieve SPARQL query results	GET	/ontology	**?query**=SPARQL_QUERY (mandatory)	RDF representation of the query results.	200,404,500
Predefined query to retrieve all models	GET	/ontology/models		RDF representation of all models.	
Predefined query to retrieve all endpoints	GET	/ontology/endpoints		RDF representation of all endpoints.	
Predefined query to retrieve all algorithms	GET	/ontology/algorithms		RDF representation of all algorithms.	
Submit SPARQL query and/or OpenTox service URL	POST	/ontology	**uri**[]=URL of a OpenTox RDF resource **query**=SPARQL_QUERY	RDF representation of the query results, if **query** is specified. if **uri[]** is specified, the server retrieves a RDF representation and adds it to the RDF storage, thus making it available for the subsequent queries.	200,404,500,502

OpenTox

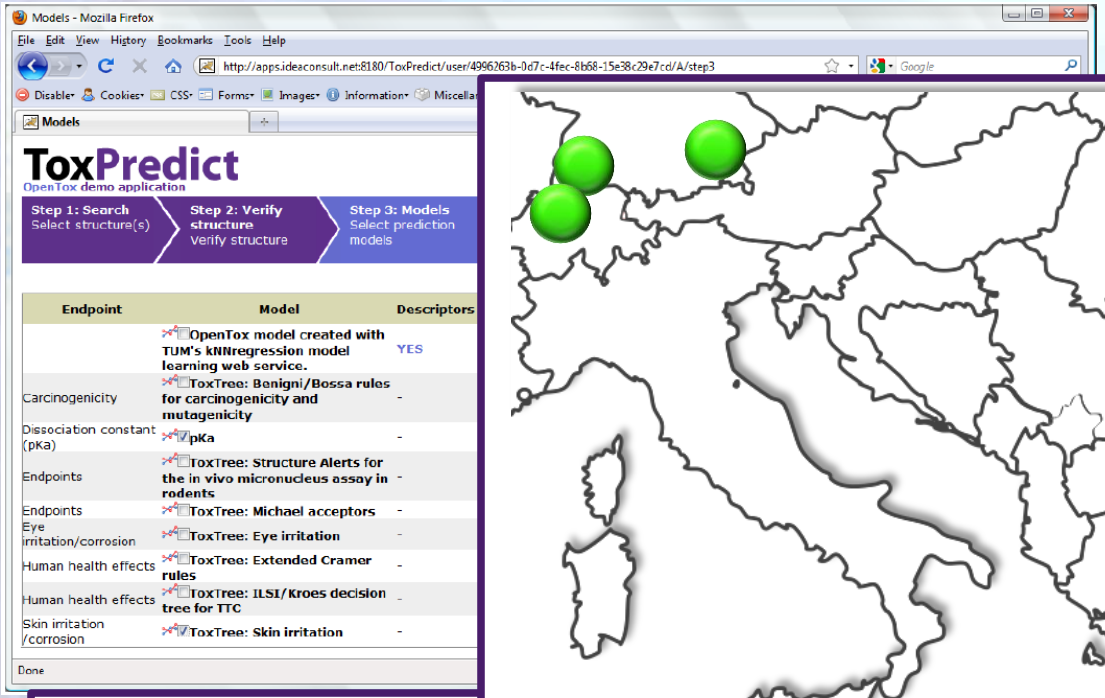
What you can do with it …



Simple building of predictive toxicology applications based on well-established methods and databases

OpenTox

What you can do with it …



Simple building c

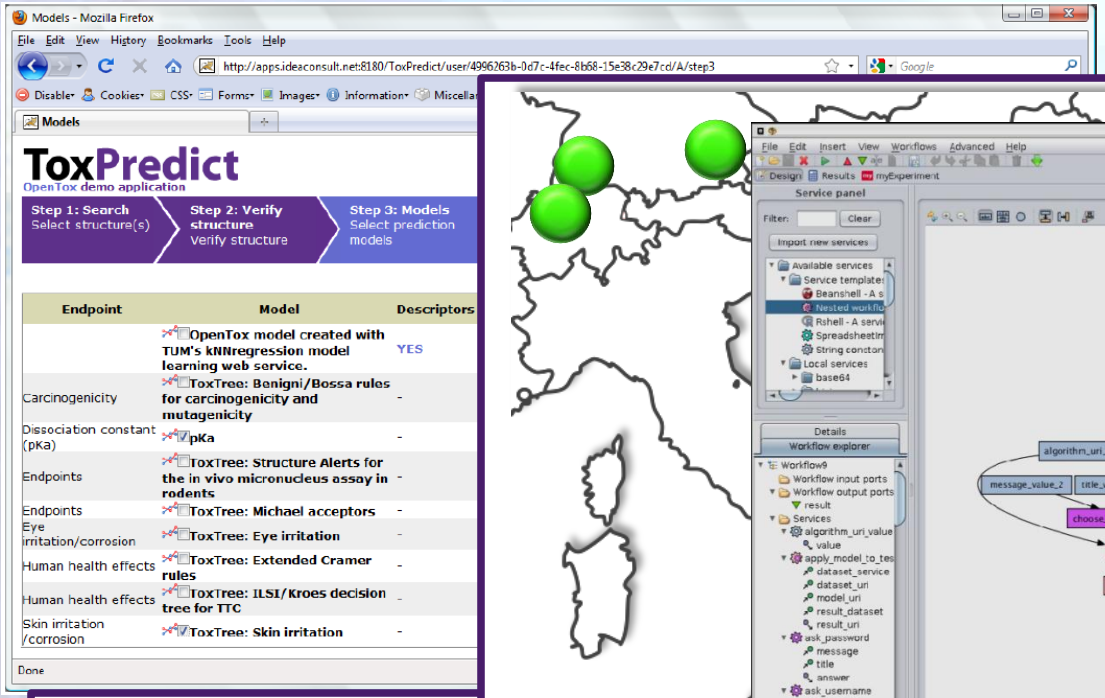
applications

methods and

Distributed applications, integrating wide range of data, models, prediction methods

OpenTox

What you can do with it …



Simple building applications methods and

Distributed wide range methods

Integration into workflow systems for computational biology

OpenTox

ToxCast

- Focus on prediction of toxicological endpoints
- Use *in vitro* data to predict *in vivo* endpoints
- Multi label approach
  - approximately 400 labels, 300 instances, 1600 features

	In vitro			*In vivo*		
Structure	ncgc_ar_agonist	ncgc_ar_antagonist	...	chr_rat_thyroid	ch_rat_liver	...
Abamectin	1	0	...	0	0	...
Acephate	0	0	...	0	1	...
Acetamiprid	1	1	...	1	0	...
...	...	...	...	...	...	...

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ToxCast: Approach and Further Steps

- Use all data available at this point, including data points with **missing values**
- Take into account interdepencies between *in vivo* endpoints (**multi-label classification**)
  - improves upon predicting endpoints individually
- Use **applicability domain** on *in vitro* data to avoid unjustified predictions
  - improves upon predicting everything
- Results comparable to other multi-label datasets
- Further steps: take into account descriptions of assays to link into biological databases

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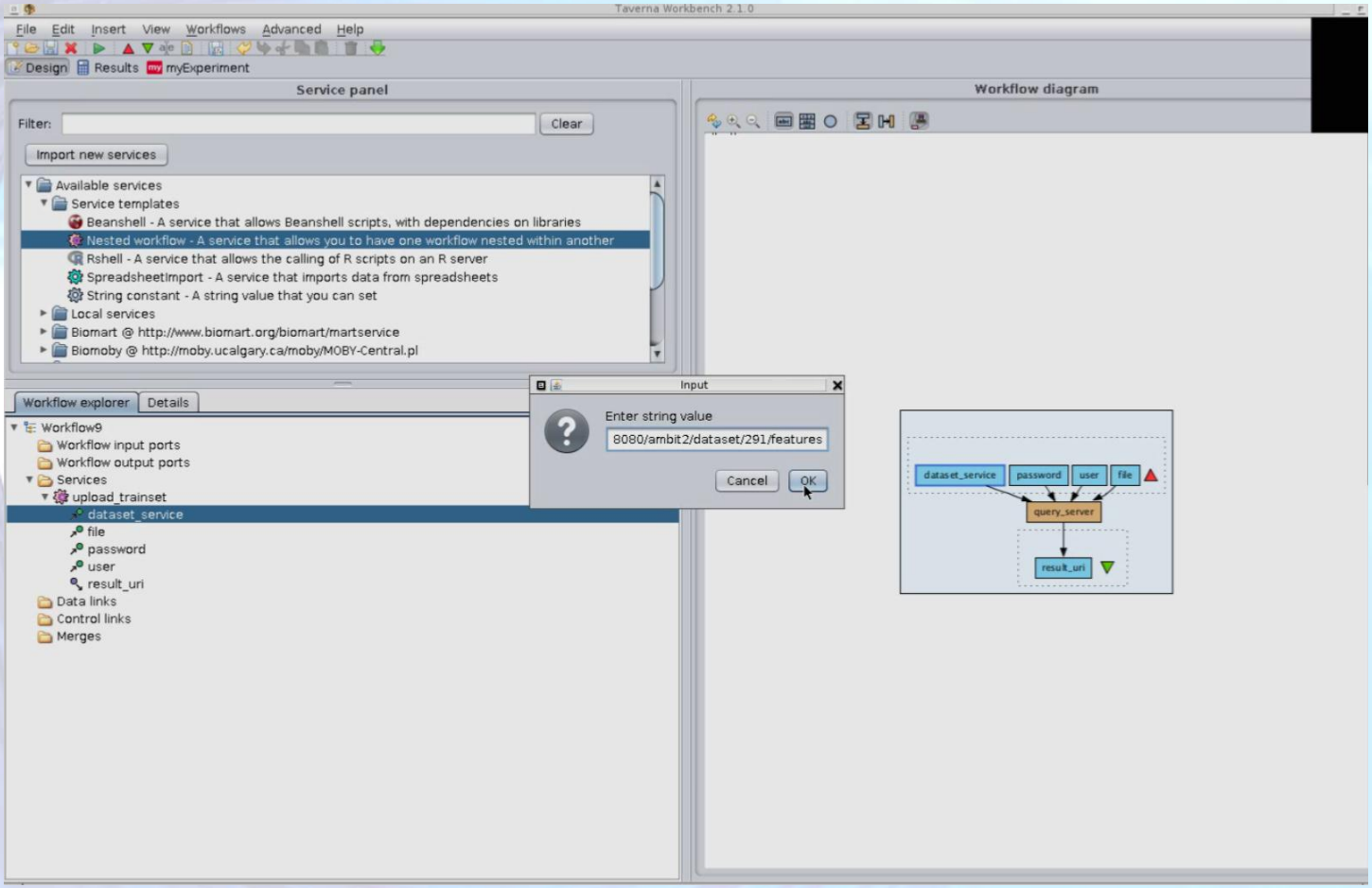
Taverna Workflow System

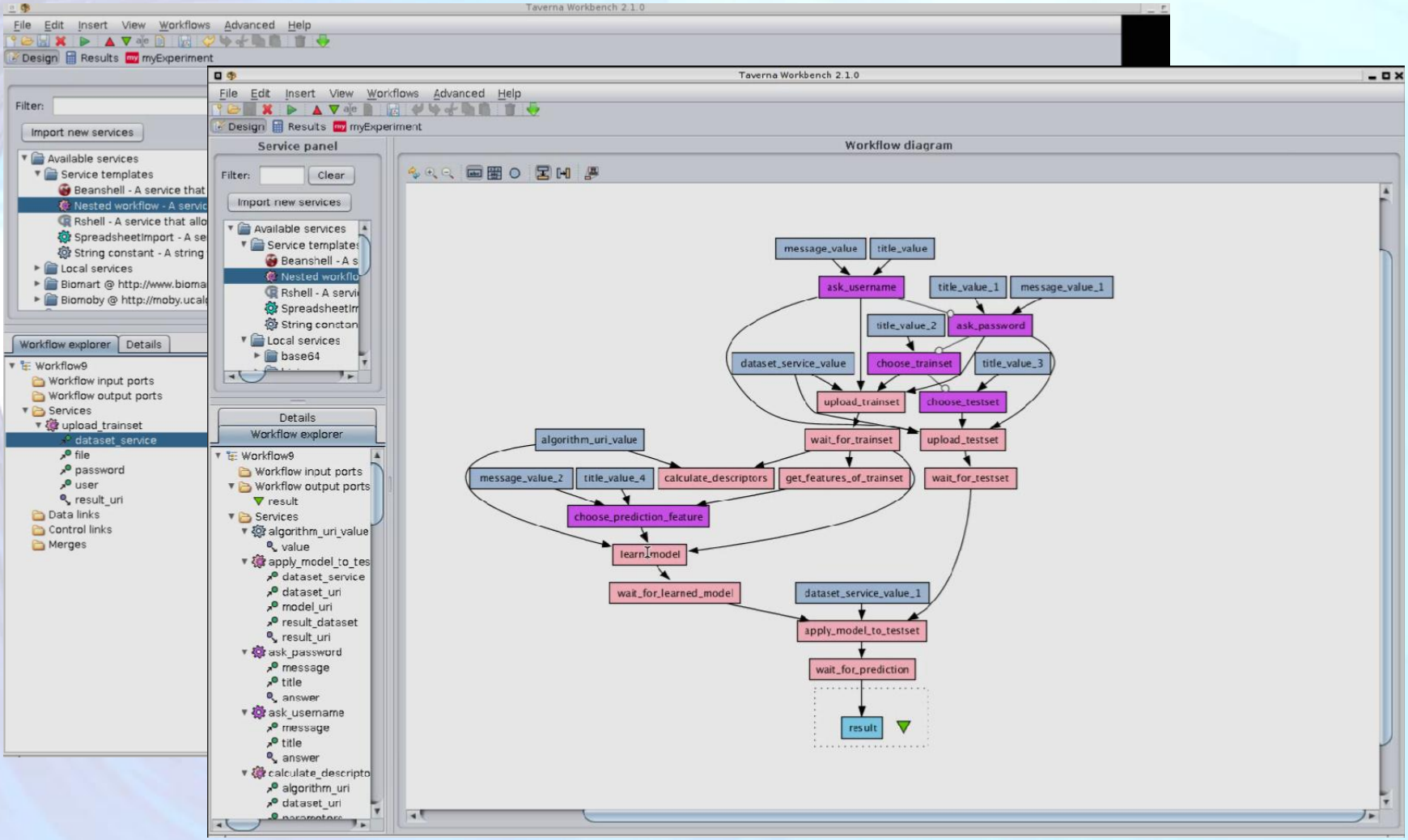
- Standard for workflows in computational biology
- OpenTox services can be integrated into Taverna workflows
- Allows for the integration of biological information
  - pathway data, …
  - mechanistic explanation

Taverna Workflow System



Test workflows will be provided for download

Taverna Workflow System



Test workflows will be provided for download

Consequences for Requirements on OpenTox

User Requirements		Software Requirements
Umambiguous data	⇒	*formal way of representing information about **data***
Unambiguous access	⇒	*well-defined interfaces*
Transparency of computational tools	⇒	*formal way of representing information about **methods**, well-defined interfaces*
Variety of user groups	⇒	*simplicity and modularity of design*
Need to integrate various resources (e.g., databases, prediction methods, models, …) to make meaningful predictions	⇒	*distributed architecture, interoperability*
Need to integrate biological information	⇒	*again, modularity of design, extensibility*

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Strategic Context/Goals

- REACH: possible reduction of test animals by using existing experimental data in conjunction with QSAR
- Also practical needs: **reporting** and form filling
- By the OECD principles,a number of requirements to a framework like OpenTox arise

	OECD Principle	OpenTox addresses by...
1	Defined Endpoint	providing a unified source of well defined and documented toxicity data with a common vocabulary
2	Unambiguous Algorithm	providing transparent access to well documented models and algorithms as well as to the source code
3	Defined Applicability Domain	integrating tools for the determination of applicability domains during the validation of prediction models
4	Goodness-of-fit, robustness and predictivity	providing scientifically sound validation routines for the determination of errors and confidences
5	Mechanistic interpretation (if possible)	integrating tools for the prediction of toxicological mechanisms and the recording of opinions and analysis in reports

OpenTox

Summary and Future Work

- Comprehensive framework for predictive toxicology that allows you to address a wide range of tasks
  - interface definitions, services (also for: validation, **reporting**, …), use cases
  - **interoperability** and **extensibility by design**
- Further work on other use cases: e.g.
  - Read Across (technical infrastructure available)
  - ToxCast
  - pathway prediction service: developing a service for predicting transformation products
  - Synergy pilot
  - …

OpenTox

OpenTox Application Demonstrations

Nina Jeliazkova (Ideaconsult, Bulgaria)
Christoph Helma (In Silico Toxicology, Switzerland)
Andreas Karwath (Albert-Ludwigs Univ. Freiburg, Germany)

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Use Cases

ToxPredict

- offers easy access for toxicological hazard estimation of a chemical structure
- for non-QSAR specialists
- a simple yet easy-to-use user interface

ToxCreate

is aimed at researchers in

- life sciences and toxicology
- QSAR experts
- people interested in machine learning/statistics
- pharmaceutical industry R&D

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ToxPredict

The use case can be divided into the following five steps:

1. Enter/select a chemical compound
2. Display selected/found structures
3. Select models
4. Perform the estimation
5. Display the results

→ **Live Demo: www.toxpredict.org**

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ToxPredict: Step 1 (behind the scenes)

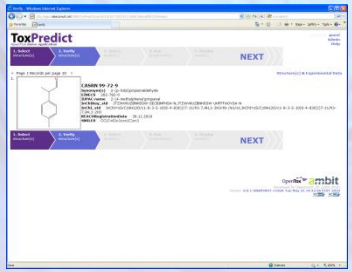
Find structure by name, registry number, SMILES, InChI, structure, substructure, similarity…

ToxPredict Web Application

OT Dataset API ***HTTP GET***

OT Ontology Service

text/uri-list,
application/rdf+xml,
chemical/x-daylight-smiles
chemical/x-mdl-sdfile,…



Here is the list of structures as URI links, RDF, MOL or SMILES.

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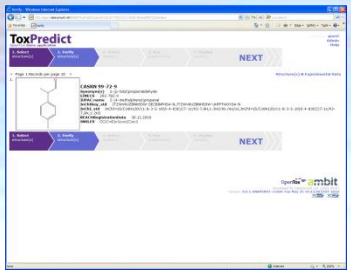
ToxPredict: Step 3 (behind the scenes)



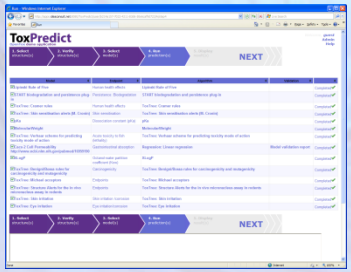
What prediction models are available? Is there a model for endpoint X?

ToxPredict Web Application

HTTP GET SPARQL query

OT Ontology Service

application/sparql-results+xml



Here is the list of model URIs and related endpoints and algorithms in SPARQL format.

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ToxCreate: intended audience

Toxicologists with

- access to toxicological data
- basic computer skills
- little or no knowledge of QSAR algorithms

Goal:

- build and validate prediction models from user provided training data

→ **Live demo** www.toxcreate.org

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Future Development

Inclusion of further QSAR algorithms

- build and validate multiple models
- automated selection of the best model (based on validation results)

GUI refinement:

- based on user feedback

Expert interface:

- access to all model building parameters
- command line/GUI versions

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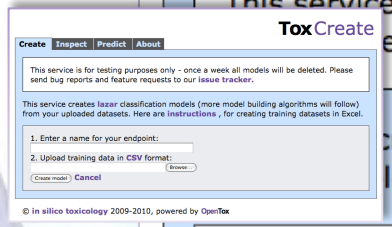
Behind the Scenes of ToxCreate



ToxCreate

Create | Inspect | Predict | About

This service is for testing purposes only - once a week all models will be deleted. Please
eports and feature requests to our issue tracker.

reates lazar classification models (more model building algorithms will follow)
loaded datasets. Here are instructions , for creating training datasets in Excel.

1. Enter a name for your endpoint:

2. Upload training data in CSV format:

Browse...

Create model Cancel

© in silico toxicology 2009-2010, powered by OpenTox

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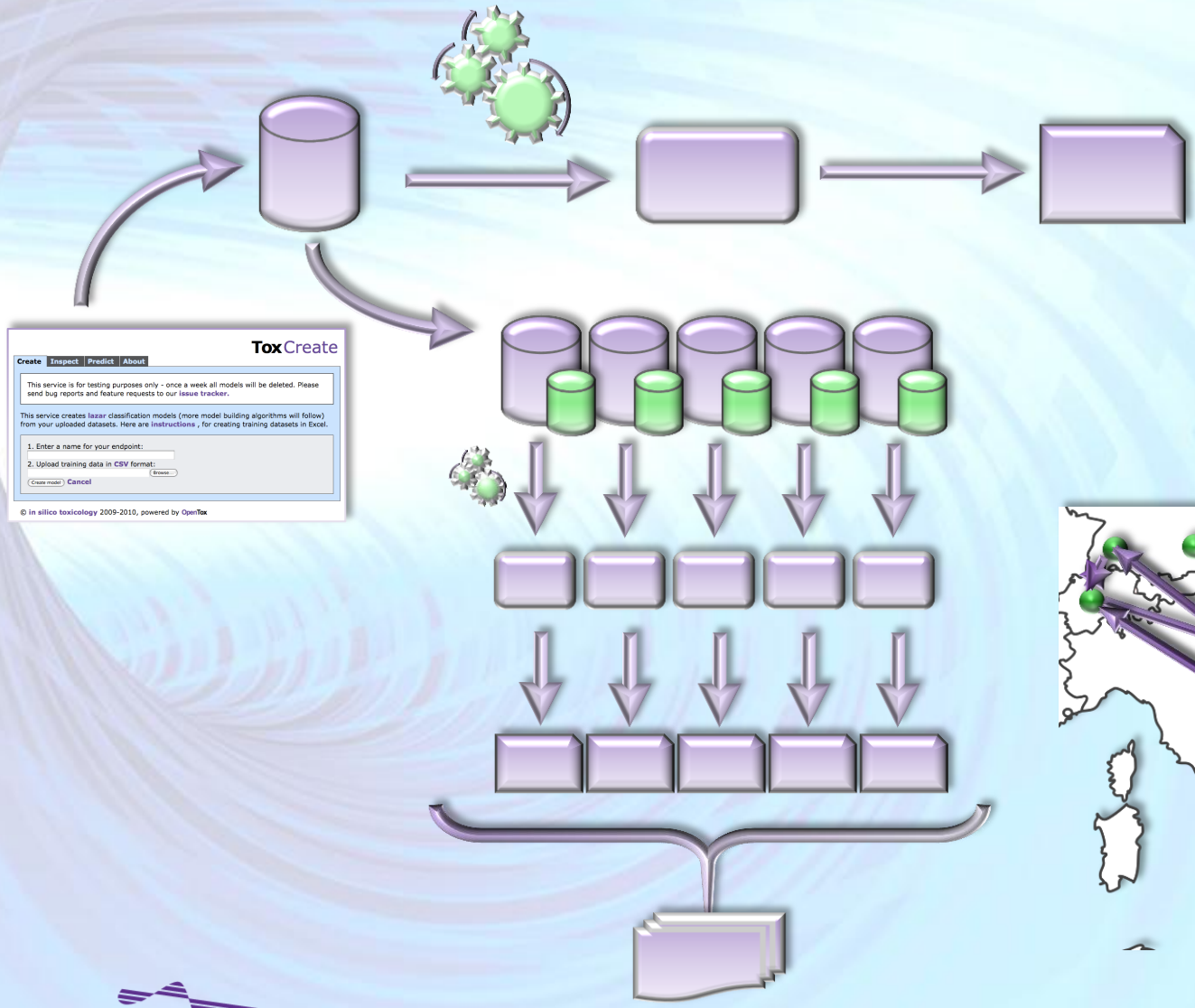
Behind the Scenes of ToxCreate



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Current State of the System

Web services online:

AlgorithmWS:	NTUA, TUM, IDEA, IST
ModelWS:	NTUA, TUM, IDEA, IST
FeatureWS:	NTUA, TUM, IDEA, IST, ALU-FR
CompoundWS:	NTUA, TUM, IDEA, IST
ValidationWS:	ALU-FR
DatasetWS:	NTUA, TUM, IDEA, IST, ALU-FR

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Collaboration, Sustainability & Future Directions

Barry Hardy

Douglas Connect

OpenTox Project Coordinator

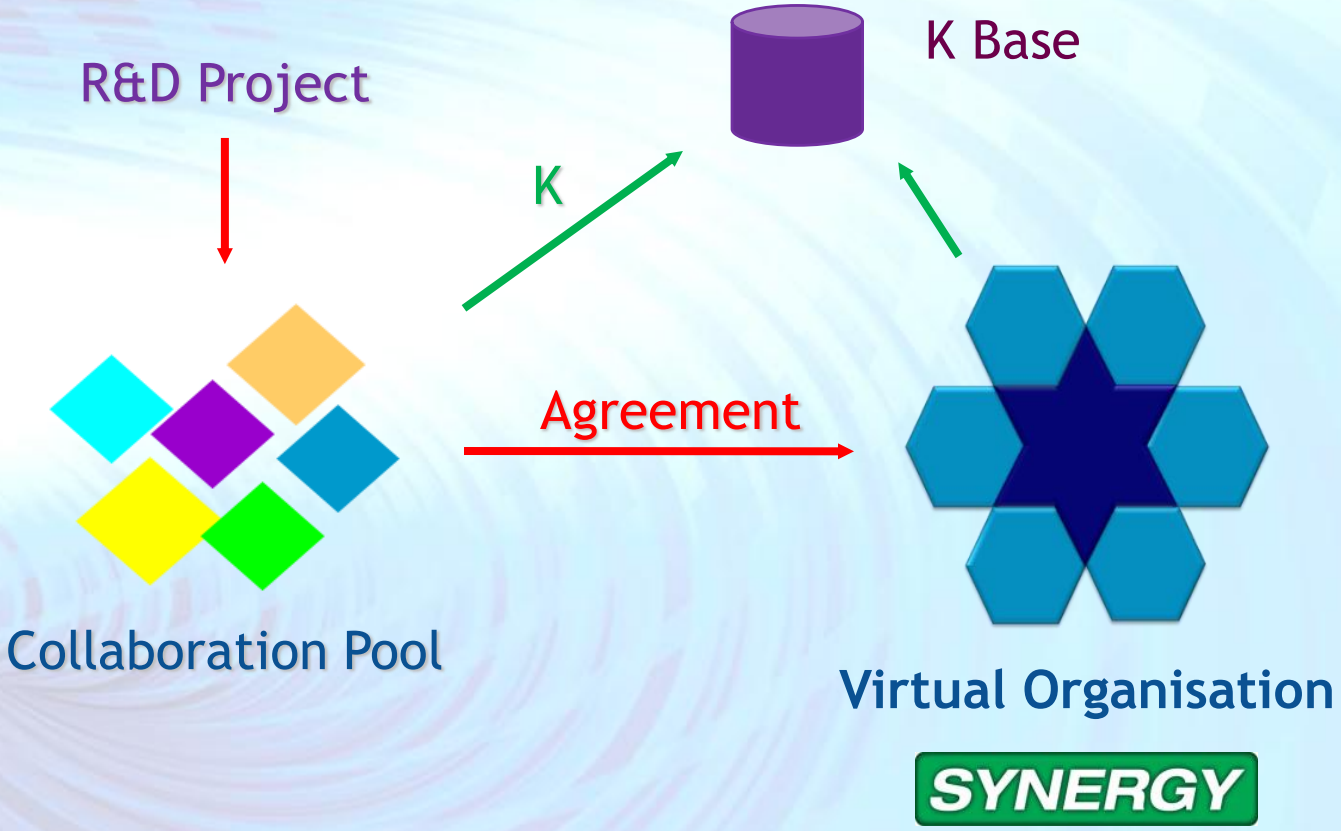
OpenTox

Our Drivers – Taking on Technical, Cultural and "Other" Challenges of the Unexpected

Visit with Lions at Mukuni Reintroduction Project, Livingstone, Zambia

OpenTox

Virtual Organisation Pilots



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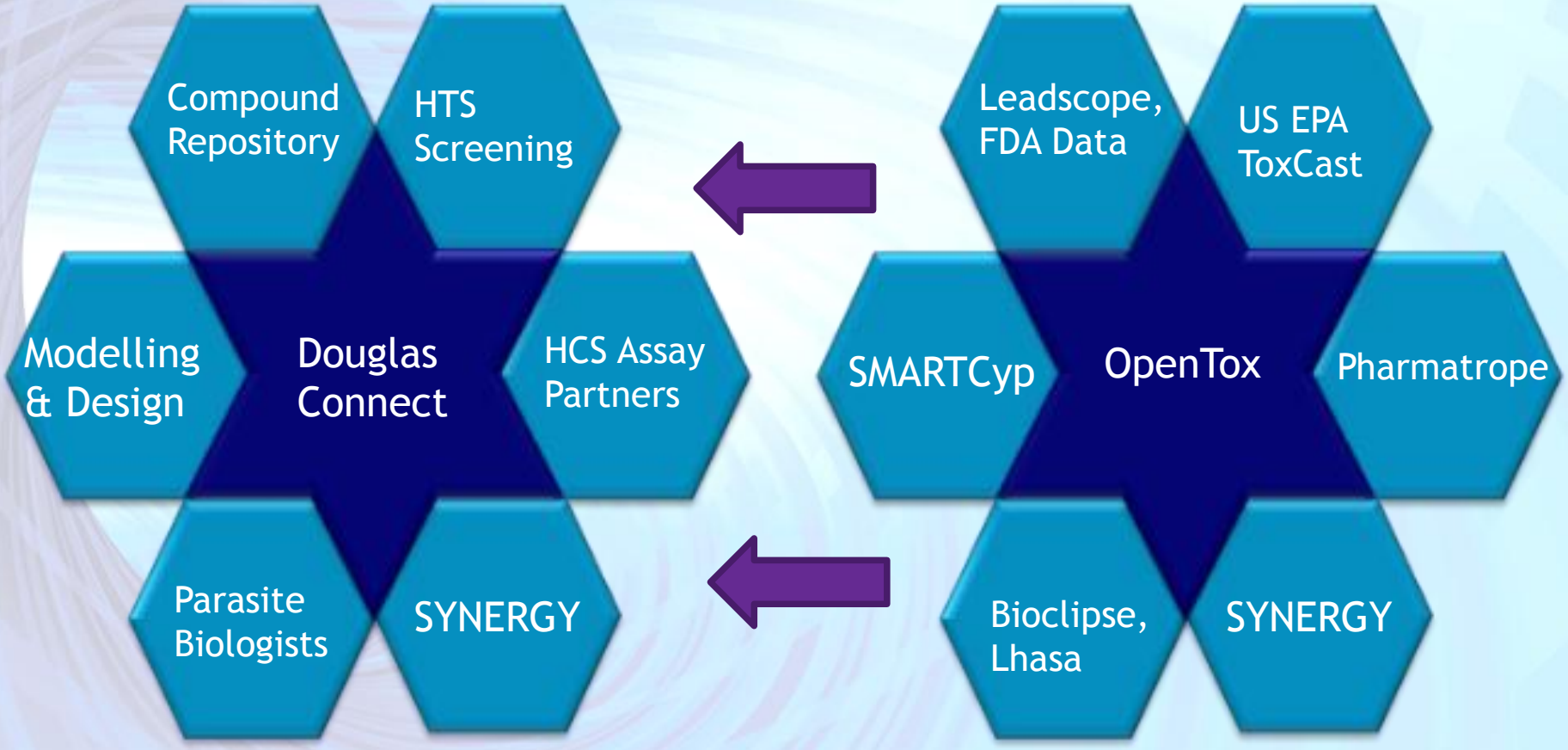
Virtual Organisation Pilots



Neglected Disease Drug Design VO

Predictive Toxicology VO

OpenTox

OpenTox - Synergy Predictive Toxicology VO Pilot Strategy Development & Case Study

1. Data Mining of Human Adverse Drug Events
   - Data Mining of Literature Knowledge
2. Creation of Mechanism-based Hypothesis
   - Selection of Biological Pathways & Targets
3. Selection of Compounds
   - Prediction of Metabolites of Compounds
4. Selection of *in vitro* assays relevant to Mechanism
   - Selection and integration of Toxicity Data
5. Creation of Predictive Toxicology Model including Model Validation and Applicability Domain
6. Selection of Low and High Content Assays for Testing in Cell Lines
   - Analysis of Results

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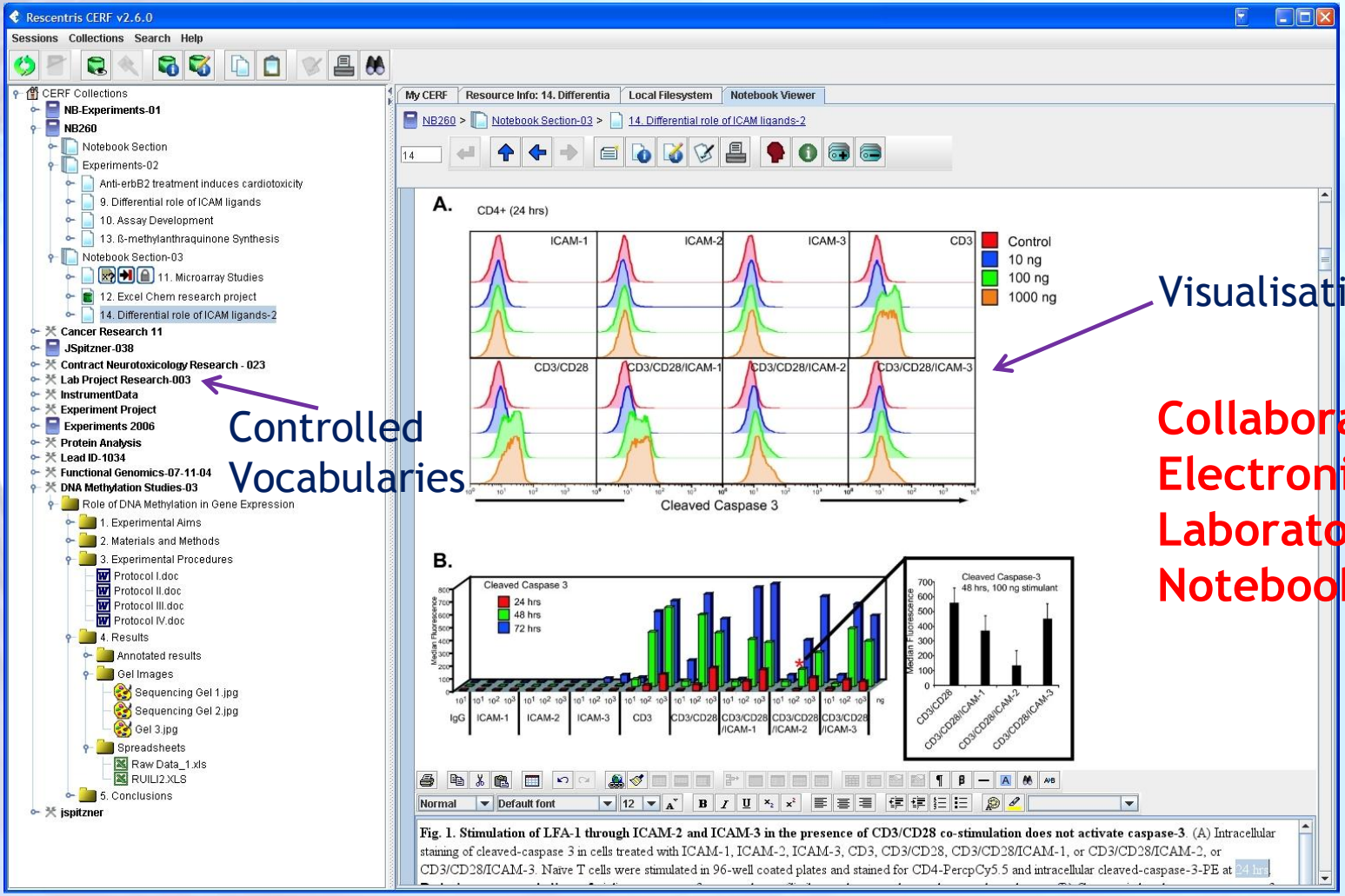
Recording of Collaborative R&D



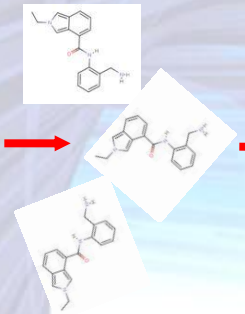
Controlled Vocabularies

Visualisation

Collaborative Electronic Laboratory Notebook (ELN)

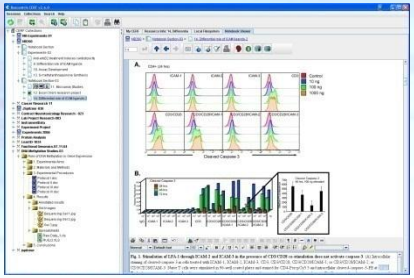
OpenTox

Synergy Collaboration Pilots

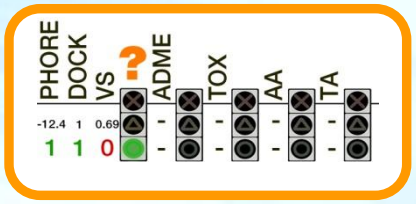


Screened Library

Data

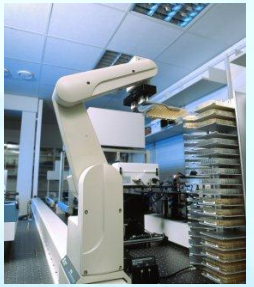


CERF

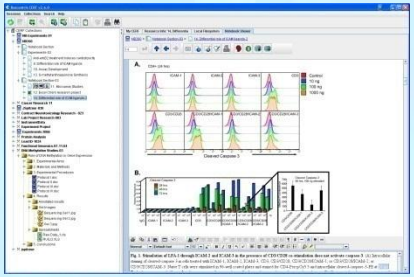


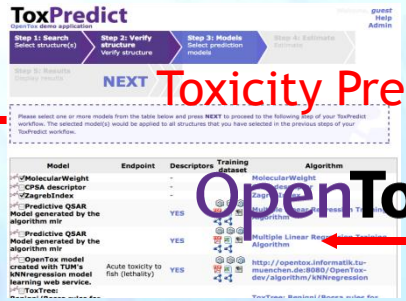
Refine Predictions

SYNERGY



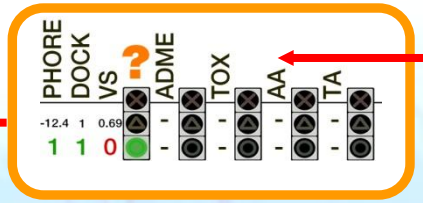
Data



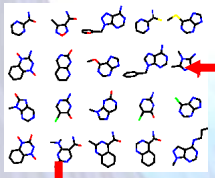


Toxicity Predictions

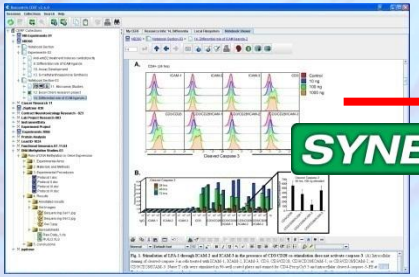
OpenTox



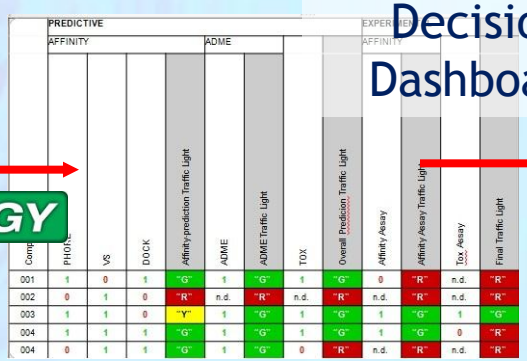
SYNERGY



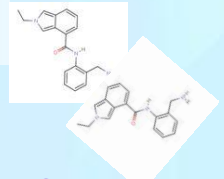
Toxicity Assays



SYNERGY



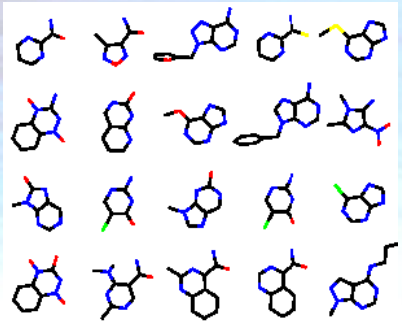
Decision Dashboard



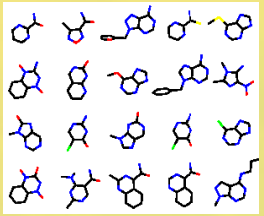
(Safer) Drug Leads

OpenTox

1. A library of compounds is entered to the ELN



ELN

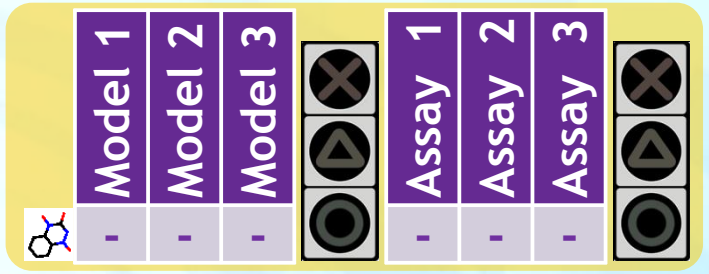


Synergy

OpenTox

2. Each compound is assigned a data structure in ELN

ELN

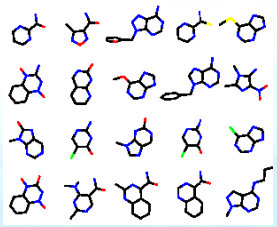


Synergy

OpenTox

OpenTox

3. ELN passes compounds to OpenTox and SYNERGY



ELN

	Model 1	Model 2	Model 3		Assay 1	Assay 2	Assay 3	
	-	-	-		-	-	-	

Synergy

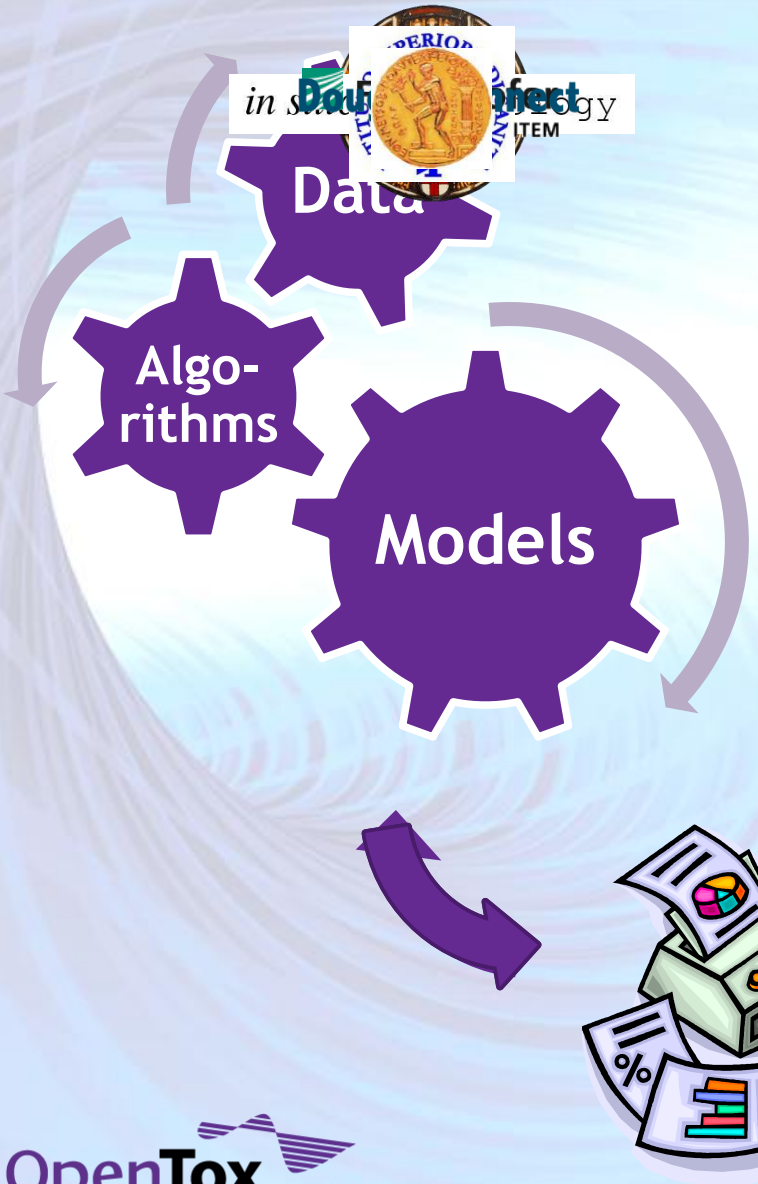
	Model 1	Model 2	Model 3		Assay 1	Assay 2	Assay 3	
	-	-	-		-	-	-	

OpenTox

	Model 1	Model 2	Model 3		Assay 1	Assay 2	Assay 3	
	-	-	-		-	-	-	

OpenTox

4. OpenTox computes toxicity predictions



ELN

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
	-	-	-	-	-	-

Synergy

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
	-	-	-	-	-	-

OpenTox

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
	1	0	1	-	-	-

OpenTox

5. OpenTox sends back a report to ELN

ELN

Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	-	-	-

Synergy

Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
-	-	-	-	-	-

OpenTox

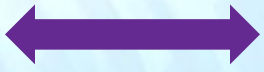
Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	-	-	-

OpenTox

6. ELN sends the results to SYNERGY

OpenTox

7. SYNERGY applies the Recommendation Rules



ELN

Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	-	-	-

Synergy

Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	-	-	-

OpenTox

8. Inconclusive data → SYNERGY calls a meeting

?

ELN

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
	1	0	1	-	-	-

Synergy

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
	1	0	1	-	-	-

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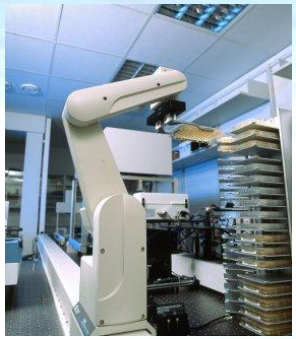
9. Experimental assays confirm toxicity



ELN

Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	-	1	1

Synergy

Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	-	-	-

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Sustainability Model

New Opportunity

K Base

K

K

Contract

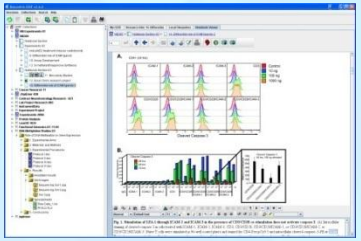
Outcomes

Predictive Toxicology Collaboration Pool

Predictive Toxicology Virtual Organization

Apps

Risk Assessments



R&D Program Services & Support

Contract Payments

PRE-CREATION

CREATION

OPERATION

TERMINATION

Service Support of Virtual Organisation Lifecycle

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In Silico Toxicology, Switzerland

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- CADASTER
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Final words...

For more information, visit

www.opentox.org

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Many thanks for your attention!

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SEVENTH FRAMEWORK PROGRAMME