

Integrating Predictive Toxicology Model Development

SMi ADMET Conference

7,8 July 2010

London, UK

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Collaborative Predictive Toxicology Challenge

Input Structure



Out - Toxic or Not?

- LD50
- Liver Toxicity
- Secondary Metabolites
- Bioavailability
- Mutagenicity
- Carcogenicity
- Reproductive Toxicology
- Skin Irritation
- Aqua Toxicity
- Combined predictions for arrays of multiple end points



Driver



Increasing demands on industry to satisfy safety evaluation and risk assessment required by REACH legislation. (Over 142k cmpds registered).

Step 1: Search
Select structure(s)

Step 2: Verify structure
Verify structure

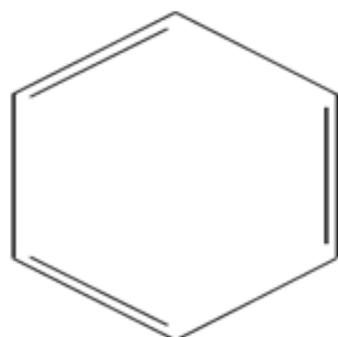
Step 3: Models
Select prediction models

Step 4: Estimate
Estimate

Step 5: Results
Display results

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
EINECS
IUPAC name
Synonym

71-43-2
200-753-7
benzene
(6)annulene; benzine; Benzol; Benzolene;
bicarburet of hydrogen; carbon oil; Coal naphtha;
cyclohexatriene; mineral naphtha; motor benzol;
nitration benzene; Phene; Phenyl hydride;
pyrobenzol.

Synonym
Synonym
Synonym
Quality label

21742.0
Benzene
benzene
OK

MolecularWeight  **MolecularWeight**

MW

78.1112

Development of Strategies for Interoperable Resources & Applications in Predictive Toxicology



Eliminate
traditional
circus acts,
animals



Create
theatrical
themes,
storylines,
new acts

**Blue
Ocean**

Reduce
dangerous acts,
traditional
humour,
transport costs

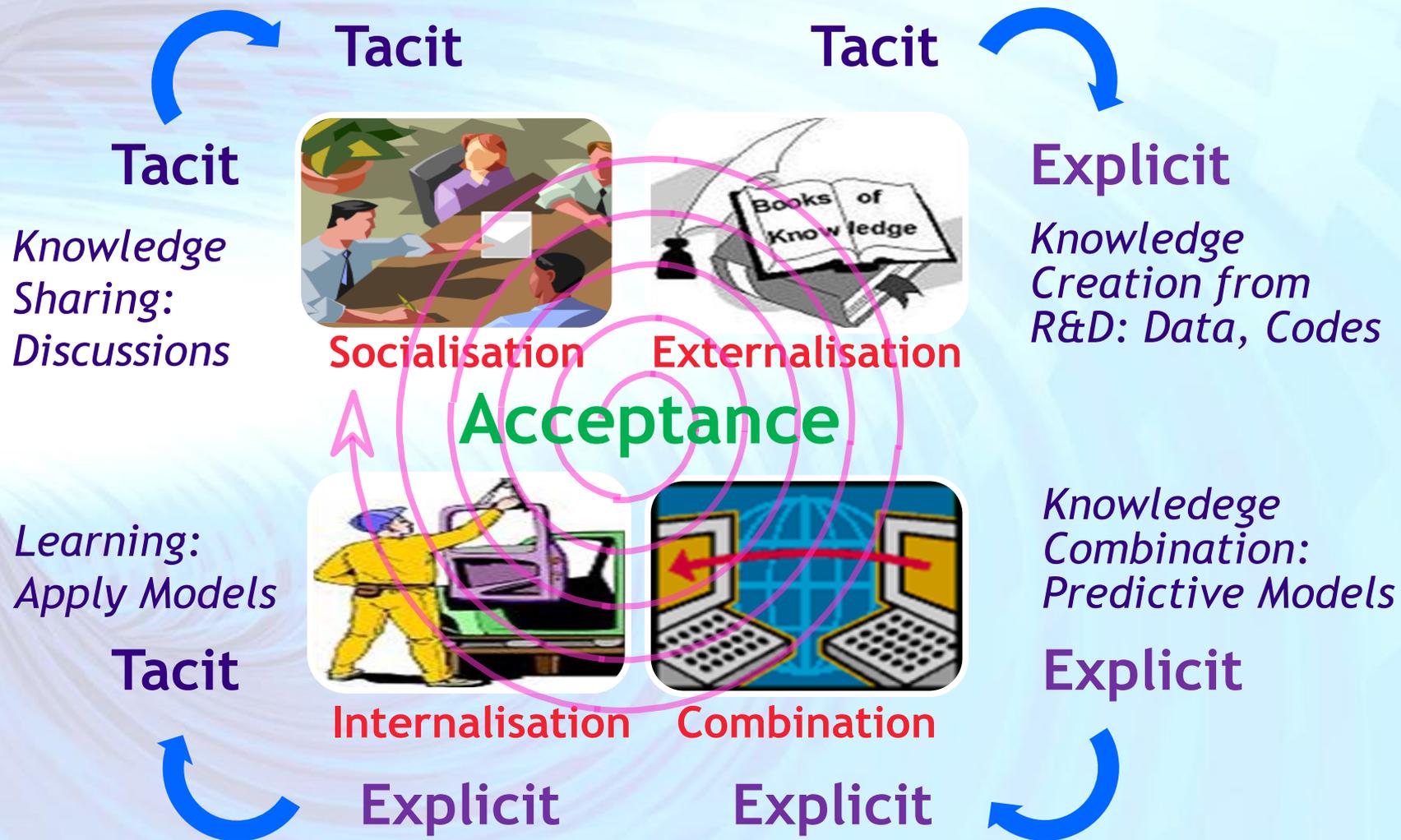


Raise
tent standards,
artistic
sophistication,
ticket prices!



Based on Blue Ocean Strategy,
Kim & Mauborne 2006

SECI Model for Knowledge Management



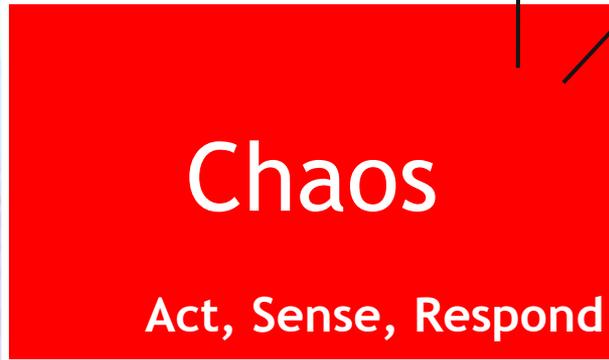
Complexity Context

Non Repeatable
Adaptative, Patterns,
Filters

Sense
Making for
Emergent
Practice

Leadership
Novel
Practice

Lack of Cause & Effect, Stability-focused
Intervention, Crisis Management



Complex Cause & Effect
Systems Thinking, Analysis

Processes
Good
Practice

Procedures
Best
Practice

Cause & Effect
Repeatable, SOPs



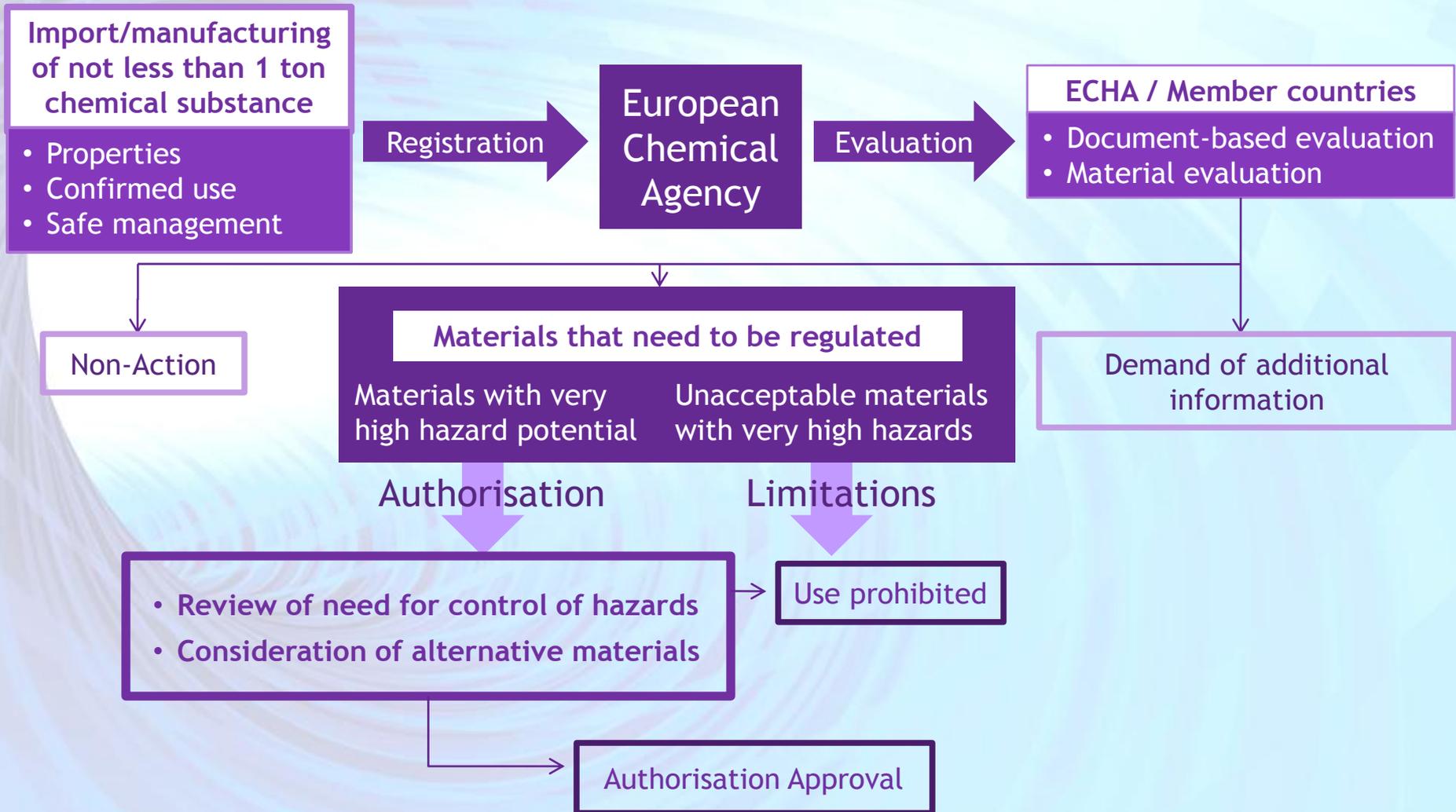
REACH

An aerial photograph of a lush green landscape, possibly a park or a rural area, viewed through a black grid pattern. The word "REACH" is written in large, white, sans-serif capital letters across the center of the image.

REACH

(enRegistrement, Evaluation et
Autorisation des substances CHimiques)

REACH Registration



Accelerating Knowledge Flows in Predictive Toxicology

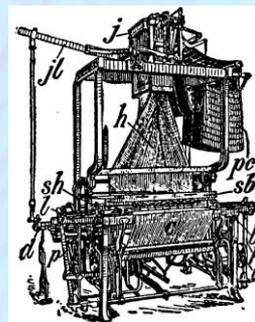
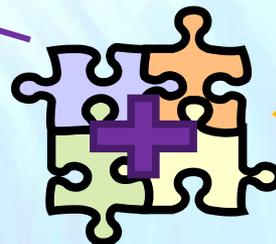
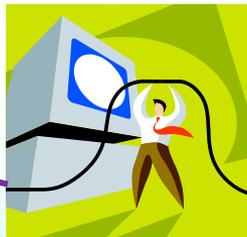
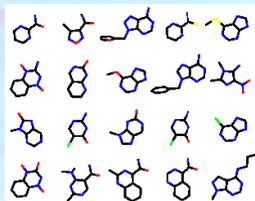
ToxPredict

Step 1: Search (find structure)
 Step 2: Verify (verify structure)
 Step 3: Models (model generation)
 Step 4: Evaluate (evaluate model)

Model

Model	Endpoint	Descriptors	Training dataset	Algorithm
MolecularWeight	-	-	-	MolecularWeight
CPSA descriptor	-	-	-	CPSA descriptor
QsarsIndex	-	-	-	QsarsIndex
Predictive QSAR Model generated by the algorithm mlr	YES	+	+	Multiple Linear Regression Training Algorithm
Predictive QSAR Model generated by the algorithm mlr	YES	+	+	Multiple Linear Regression Training Algorithm
Quantile model created with TUM's MLRegression model learning web service.	Acute toxicity to fish (lethality)	+	+	http://opentox.informatik.tum.de/algorithm/mlrregression

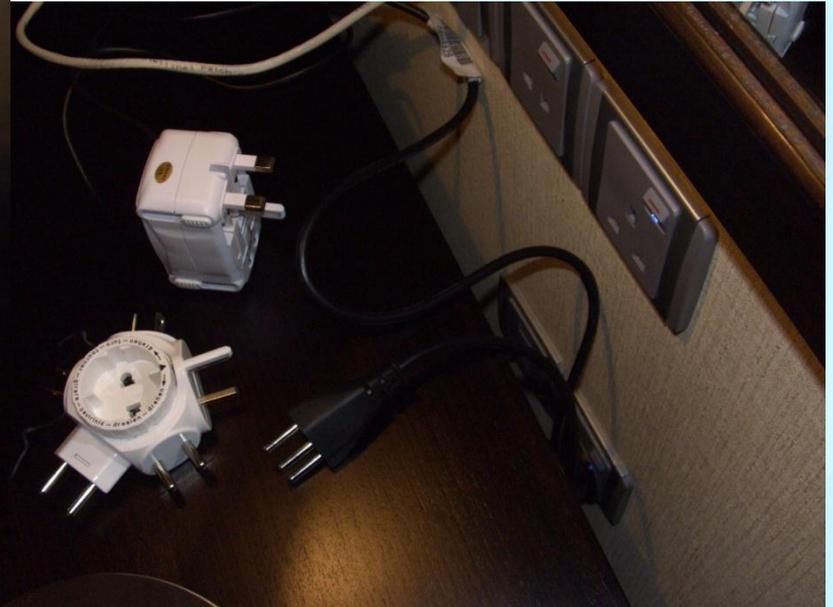
Toxicity Predictions



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

Absence of Interoperability creates Problems



Adaptor Challenge in Jeddah, 2008

Interacting Components create Solutions



Adaptor Solution in Jeddah, 2008

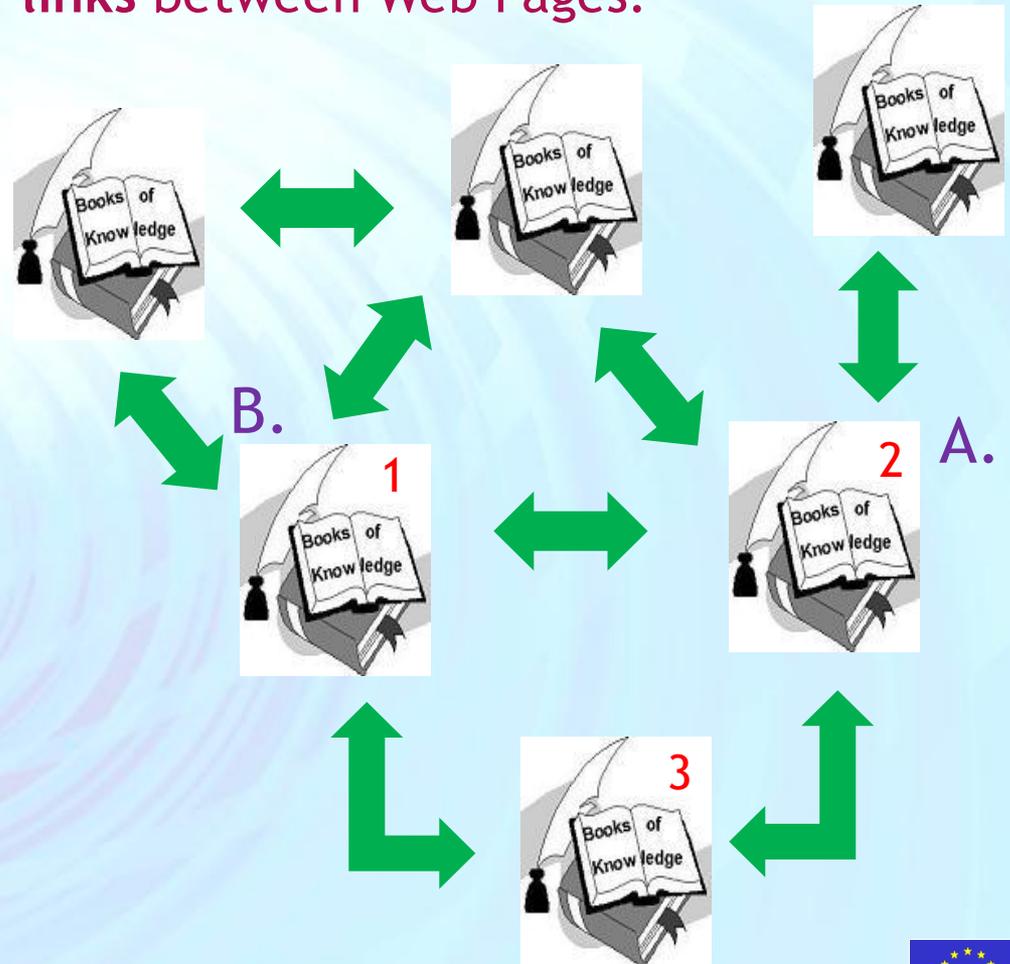
Value is in Linking

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

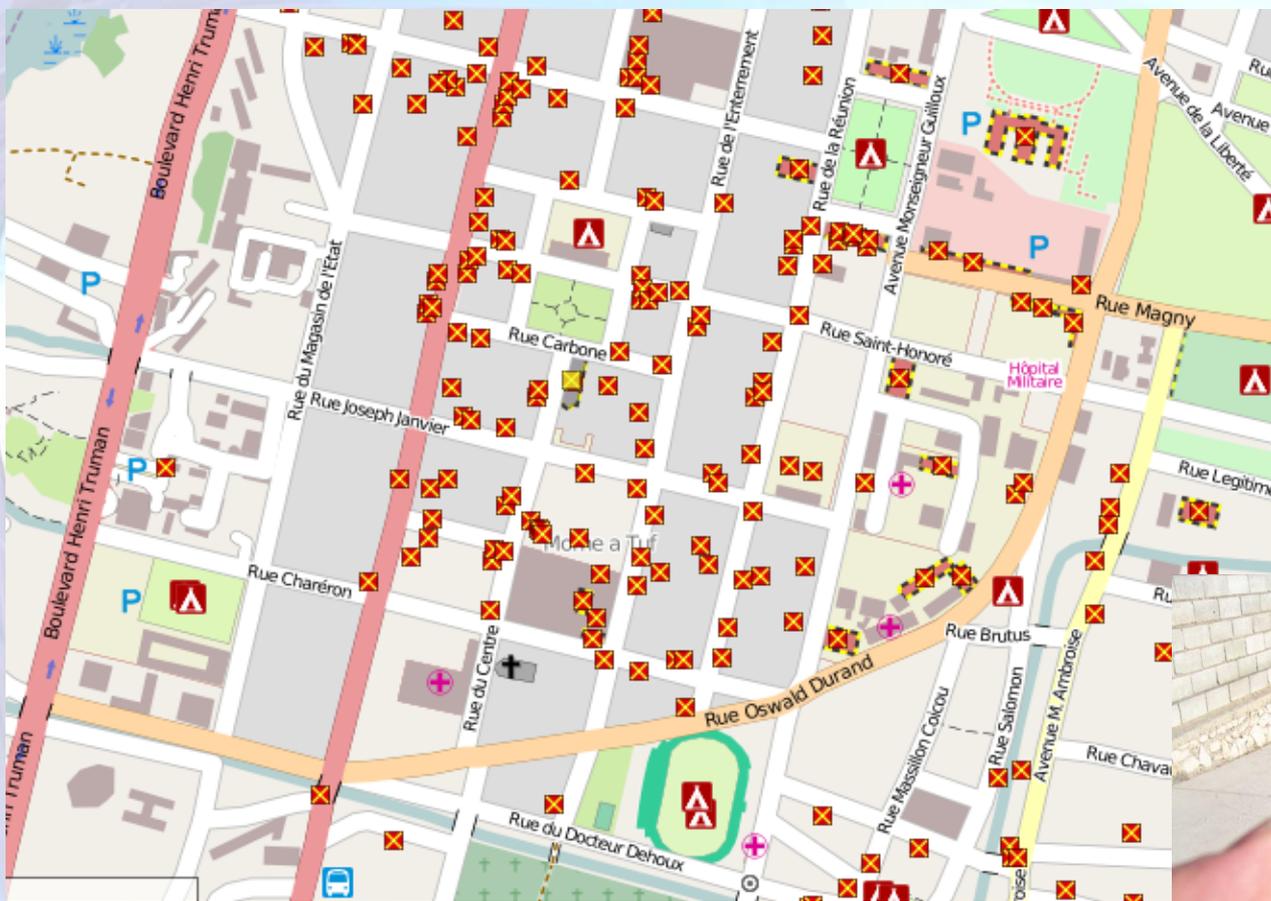
Page Ranking

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



Solution created by Linked Open Data, Web Applications and Crowdsourcing



Haiti Earthquake Crisis Response (2010)

wiki.openstreetmap.org

OpenTox is an Integrating Framework

Framework

- Toxicity Data (Linked)
- *in silico* models
- Validation & Reporting
- Interpretation aids

Diverse Access

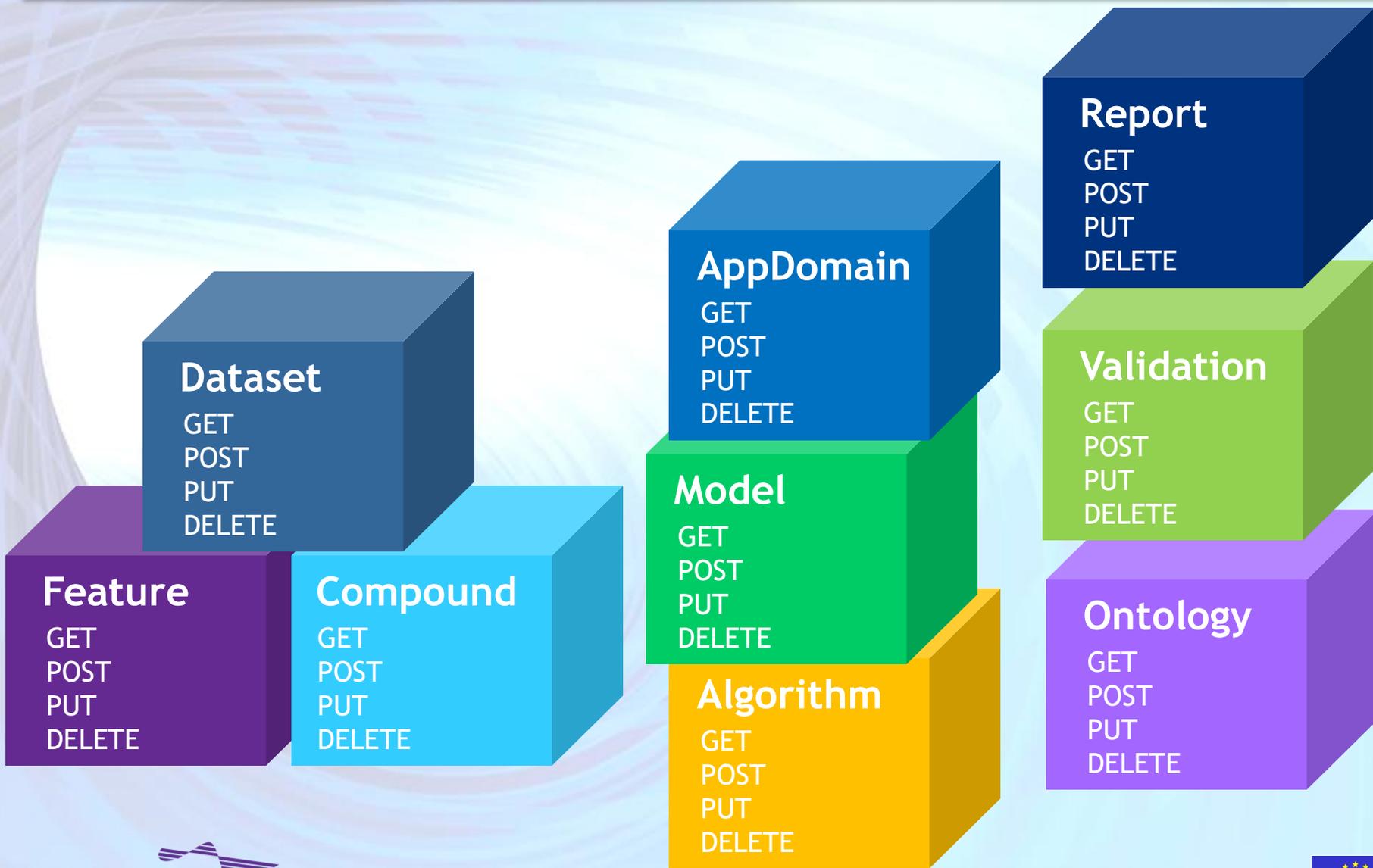
- Toxicologist, Biologist, Chem - ists
- Computational Scientists
- Interfaces for new algorithm development & integration

Interoperability

- Promote Standards
- Core Open Source Components
- Support Ontologies & Integration of Multiple Resources

	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 inference, correlation or prediction of toxicological mechanisms and the recording of opinions and analysis in reports

Overview of Application Programming Interfaces



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

OpenTox Interface Definition Example

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

www.opentox.org/dev/apis

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.



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

OpenTox
Ontology Working Group

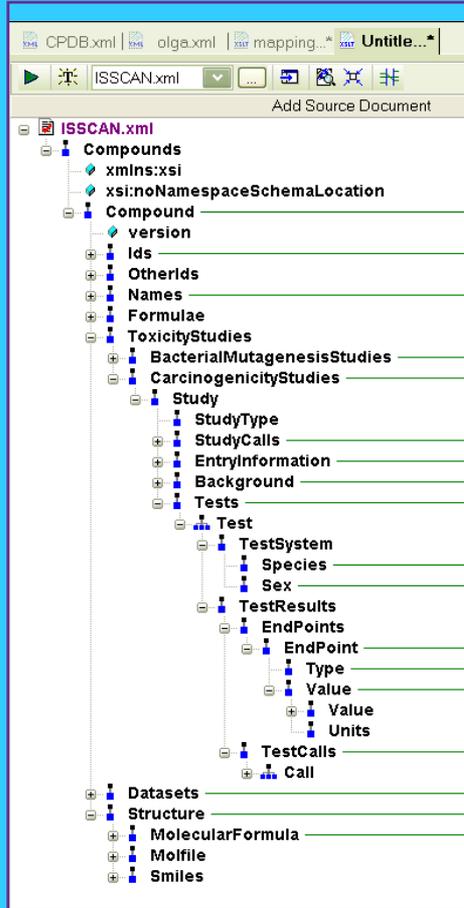
The screenshot shows a 'CLASS BROWSER' window for the project 'AlgorithmTypes'. The window displays a class hierarchy starting with 'owl:Thing (14)'. Underneath, the 'ota:AlgorithmType' class is expanded, showing several subclasses. The 'ota:Learning' class is further expanded, and 'ota:Classification (4)' is highlighted. Other classes include 'ota:DescriptorCalculation', 'ota:MSDMTox', 'ota:Preprocessing', and 'ota:Utility'.

```
graph TD
    owlThing["owl:Thing (14)"]
    otaAlgorithmType["ota:AlgorithmType"]
    otaDescriptorCalculation["ota:DescriptorCalculation"]
    otaMSDMTox["ota:MSDMTox"]
    otaPreprocessing["ota:Preprocessing"]
    otaUtility["ota:Utility"]
    otaPatternMining["ota:PatternMining (2)"]
    otaPharmacophoreGeneration["ota:PharmacophoreGeneration"]
    otaPhysicoChemical["ota:PhysicoChemical"]
    otaQuantumChemical["ota:QuantumChemical"]
    otaSimilarityDistance["ota:SimilarityDistance"]
    otaTopological["ota:Topological"]
    otaClustering["ota:Clustering"]
    otaLearning["ota:Learning"]
    otaClassification["ota:Classification (4)"]
    otaEagerLearning["ota:EagerLearning (4)"]
    otaLazyLearning["ota:LazyLearning (4)"]
    otaRegression["ota:Regression (4)"]
    otaMultipleTargets["ota:MultipleTargets (4)"]
    otaRules["ota:Rules"]
    otaSingleTarget["ota:SingleTarget (4)"]
    otaDataCleanup["ota:DataCleanup"]
    otaDiscretization["ota:Discretization (2)"]
    otaFeatureSelection["ota:FeatureSelection (2)"]
    otaNormalization["ota:Normalization"]
    otaSemiSupervised["ota:SemiSupervised"]
    otaSupervised["ota:Supervised (11)"]
    otaUnsupervised["ota:Unsupervised (3)"]
    otaGeneration3D["ota:Generation3D"]
    otaSimilarityDistanceCalculation["ota:SimilarityDistanceCalculation"]
    otaVisualisation["ota:Visualisation"]

    owlThing --- otaAlgorithmType
    otaAlgorithmType --- otaDescriptorCalculation
    otaAlgorithmType --- otaMSDMTox
    otaAlgorithmType --- otaPreprocessing
    otaAlgorithmType --- otaUtility
    otaDescriptorCalculation --- otaPatternMining
    otaDescriptorCalculation --- otaPharmacophoreGeneration
    otaDescriptorCalculation --- otaPhysicoChemical
    otaDescriptorCalculation --- otaQuantumChemical
    otaDescriptorCalculation --- otaSimilarityDistance
    otaDescriptorCalculation --- otaTopological
    otaMSDMTox --- otaClustering
    otaMSDMTox --- otaLearning
    otaLearning --- otaClassification
    otaLearning --- otaEagerLearning
    otaLearning --- otaLazyLearning
    otaLearning --- otaRegression
    otaLearning --- otaMultipleTargets
    otaLearning --- otaRules
    otaLearning --- otaSingleTarget
    otaPreprocessing --- otaDataCleanup
    otaPreprocessing --- otaDiscretization
    otaPreprocessing --- otaFeatureSelection
    otaPreprocessing --- otaNormalization
    otaUtility --- otaGeneration3D
    otaUtility --- otaSimilarityDistanceCalculation
    otaUtility --- otaVisualisation
```

Toxicological Endpoint Ontology Development

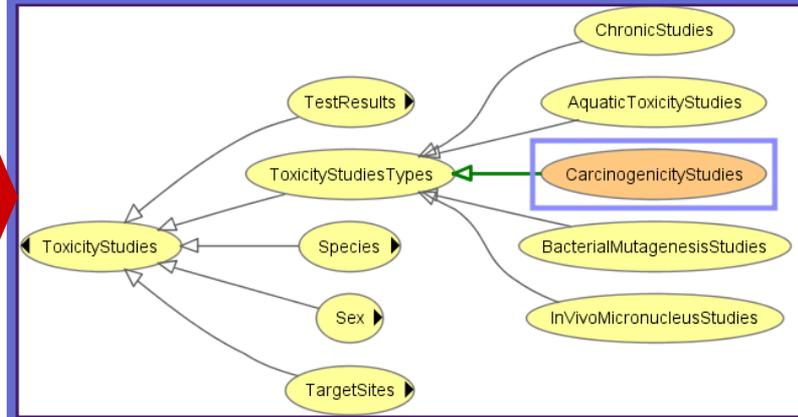
ToxML schema



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

OpenTox
Toxicological
Endpoint
Ontology

Ontology Development



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

Collaborative
Protégé
Environment

OpenToxipedia



Barry Hardy Log out Quicktools Site Setup Help

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Contents View Edit Rules Sharing History

Actions Display Add new... State: Published

OpenToxipedia

by Barry Hardy — last modified Sep 03, 2009 01:09 PM

OpenTox Community Resource for Toxicology Vocabulary and Ontology

OpenTox is supporting the creation and curation of OpenToxipedia, a community-based predictive toxicology knowledge resource. All members of the community are welcome to provide entries, suggested definition edits or additional information to entries in the resource.

OpenTox is supporting the application and development of the **ToxML** standard for representation of toxicology data, the **OECD principles for (Q)SAR model validation**, and the use of the **OECD HT** standard for regulatory reporting purposes.

OpenToxipedia provides here a Vocabulary Resource of toxicology terminology. We hope you find the resource useful and consider contributing to terms and their content.

Guidance for Vocabulary Resource entries



www.opentox.org/opentoxipedia



OpenTox: Databases

Chemical compounds - Mozilla Firefox

File Edit View History Bookmarks Tools Help

http://apps.ideaconsult.net:8180/ambit2/query/smarts?type=smiles&search=[*]OC(=O)[%236%3BH1]%3D[%236%3BH1]c1cccc1&t

Chemical compounds

ToxPredict TTC Depiction Datasets Chemical compounds Similarity Substructure Algorithms References Features Templates Models Ontology RDF playground Help

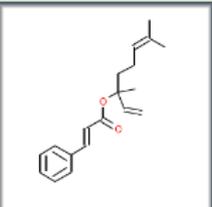
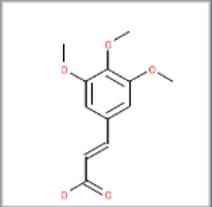
ambit

SMARTS

Keywords

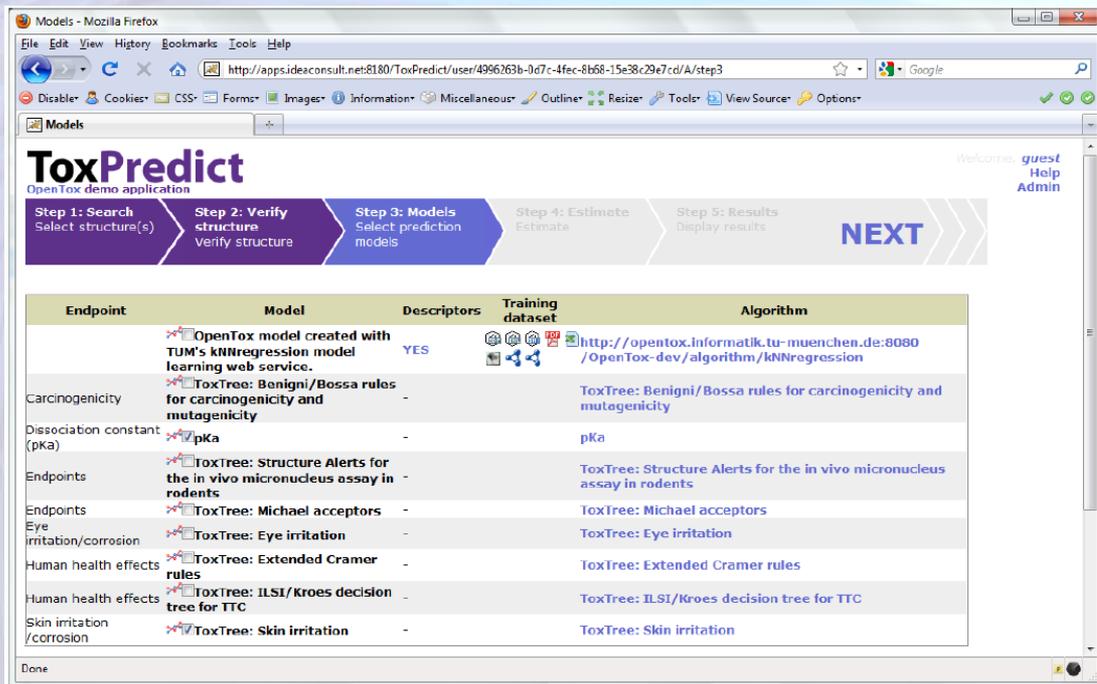
Search for substructure and properties
This site and AMBIT REST services are under development!

Retrieve data SMARTS Download as Max number of hits:

#	Compound	ECHA REGISTRATION DATE	ECHA CasRN	ECHA EC	ECHA Names	ECHA SYNONYMS	ECHA SYNONYMS	ECHA SYNONYMS	ECHA SYNONYMS	ECHA SYNONYMS	ECHA SYNONYMS
1		30.11.2010	78-37-5	201-110-3	linalyl cinnamate						
2		30.11.2010	90-50-6	201-999-8	3,4,5-trimethoxycinnamic acid						

Default
 Identifiers
 Datasets
 Models
 Endpoints
 All descriptors
 pKa
 Molecule size
 Electronic descriptors (PM3 optimized structure)
 Electronic descriptors (original structure)
 Toxtree: Cramer rules
 http://apps.idea

What you can do with it ...



ToxPredict
OpenTox demo application

Welcome, [guest](#)
[Help](#)
[Admin](#)

Step 1: Search
Select structure(s)

Step 2: Verify structure
Verify structure

Step 3: Models
Select prediction models

Step 4: Estimate
Estimate

Step 5: Results
Display results

NEXT

Endpoint	Model	Descriptors	Training dataset	Algorithm
	OpenTox model created with TUM's kNNregression model learning web service.	YES	http://opentox.informatik.tu-muenchen.de:8080/OpenTox-dev/algorithm/kNNregression	
Carcinogenicity	ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	-		ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity
Dissociation constant (pKa)	pKa	-		pKa
Endpoints	ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents	-		ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents
Endpoints	ToxTree: Michael acceptors	-		ToxTree: Michael acceptors
Eye irritation/corrosion	ToxTree: Eye irritation	-		ToxTree: Eye irritation
Human health effects	ToxTree: Extended Cramer rules	-		ToxTree: Extended Cramer rules
Human health effects	ToxTree: ILSI/Kroes decision tree for TTC	-		ToxTree: ILSI/Kroes decision tree for TTC
Skin irritation /corrosion	ToxTree: Skin irritation	-		ToxTree: Skin irritation

Done

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

What you can do with it ...



The screenshot shows the ToxPredict web application interface in a Mozilla Firefox browser window. The URL is <http://apps.ideaconsult.net:8180/ToxPredict/user/496263b-0d7c-4fec-8b68-15e38c29e7cd/A/step3>. The interface includes a navigation bar with three steps: Step 1: Search (Select structure(s)), Step 2: Verify structure (Verify structure), and Step 3: Models (Select prediction models). Below the navigation bar is a table with columns for Endpoint, Model, and Descriptors.

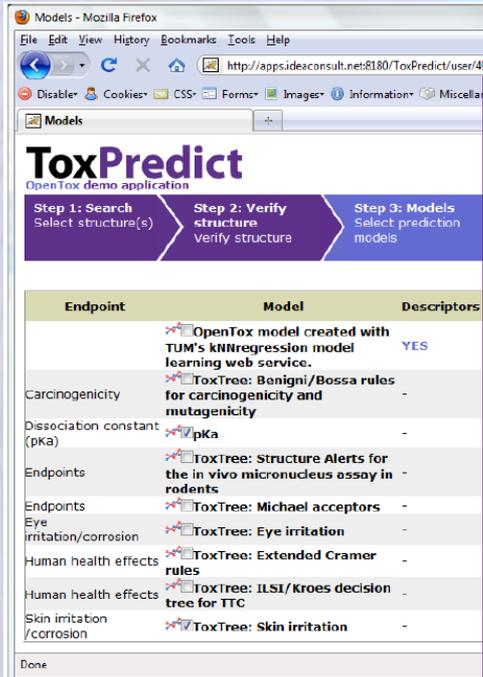
Endpoint	Model	Descriptors
	<input checked="" type="checkbox"/> OpenTox model created with TUM's kNNregression model learning web service.	YES
Carcinogenicity	<input checked="" type="checkbox"/> ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	-
Dissociation constant (pKa)	<input checked="" type="checkbox"/> pKa	-
Endpoints	<input checked="" type="checkbox"/> ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents	-
Endpoints	<input checked="" type="checkbox"/> ToxTree: Michael acceptors	-
Eye irritation/corrosion	<input checked="" type="checkbox"/> ToxTree: Eye irritation	-
Human health effects	<input checked="" type="checkbox"/> ToxTree: Extended Cramer rules	-
Human health effects	<input checked="" type="checkbox"/> ToxTree: ILSI/Kroes decision tree for TTC	-
Skin irritation/corrosion	<input checked="" type="checkbox"/> ToxTree: Skin irritation	-

Overlaid on the right side of the screenshot is a map of Europe with five green circular markers placed at various geographical locations: two in the north (Germany/Poland area), one in the east (Russia/Ukraine area), one in the south (Spain/Italy area), and one in the southwest (Ireland area).

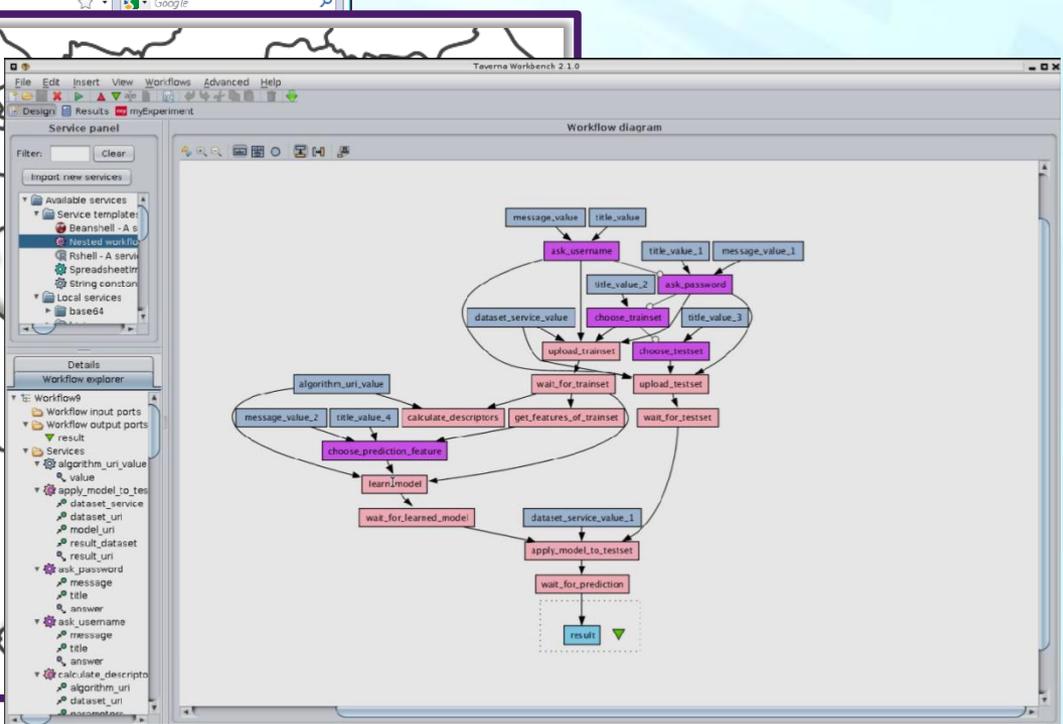
Simple building of applications methods and

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

What you can do with it ...



Endpoint	Model	Descriptors
	OpenTox model created with TUM's kNN regression model learning web service.	YES
Carcinogenicity	ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	-
Dissociation constant (pKa)	pKa	-
Endpoints	ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents	-
Endpoints	ToxTree: Michael acceptors	-
Eye irritation/corrosion	ToxTree: Eye irritation	-
Human health effects	ToxTree: Extended Cramer rules	-
Human health effects	ToxTree: ILSI/Kroes decision tree for TTC	-
Skin irritation/corrosion	ToxTree: Skin irritation	-



The workflow diagram in Taverna shows a sequence of tasks: 'ask_username' and 'ask_password' for user authentication; 'choose_trainset' and 'choose_testset' for dataset selection; 'upload_trainset' and 'upload_testset' for data upload; 'wait_for_trainset' and 'wait_for_testset' for data processing; 'calculate_descriptors' and 'get_features_of_trainset' for feature extraction; 'learn_model' for model training; 'wait_for_learned_model' for model availability; 'apply_model_to_testset' for model application; and 'wait_for_prediction' for final results.

Simple building of applications methods and

Distributed of wide range of methods

Integration into workflow systems for computational biology

Workflows Connecting OpenTox services

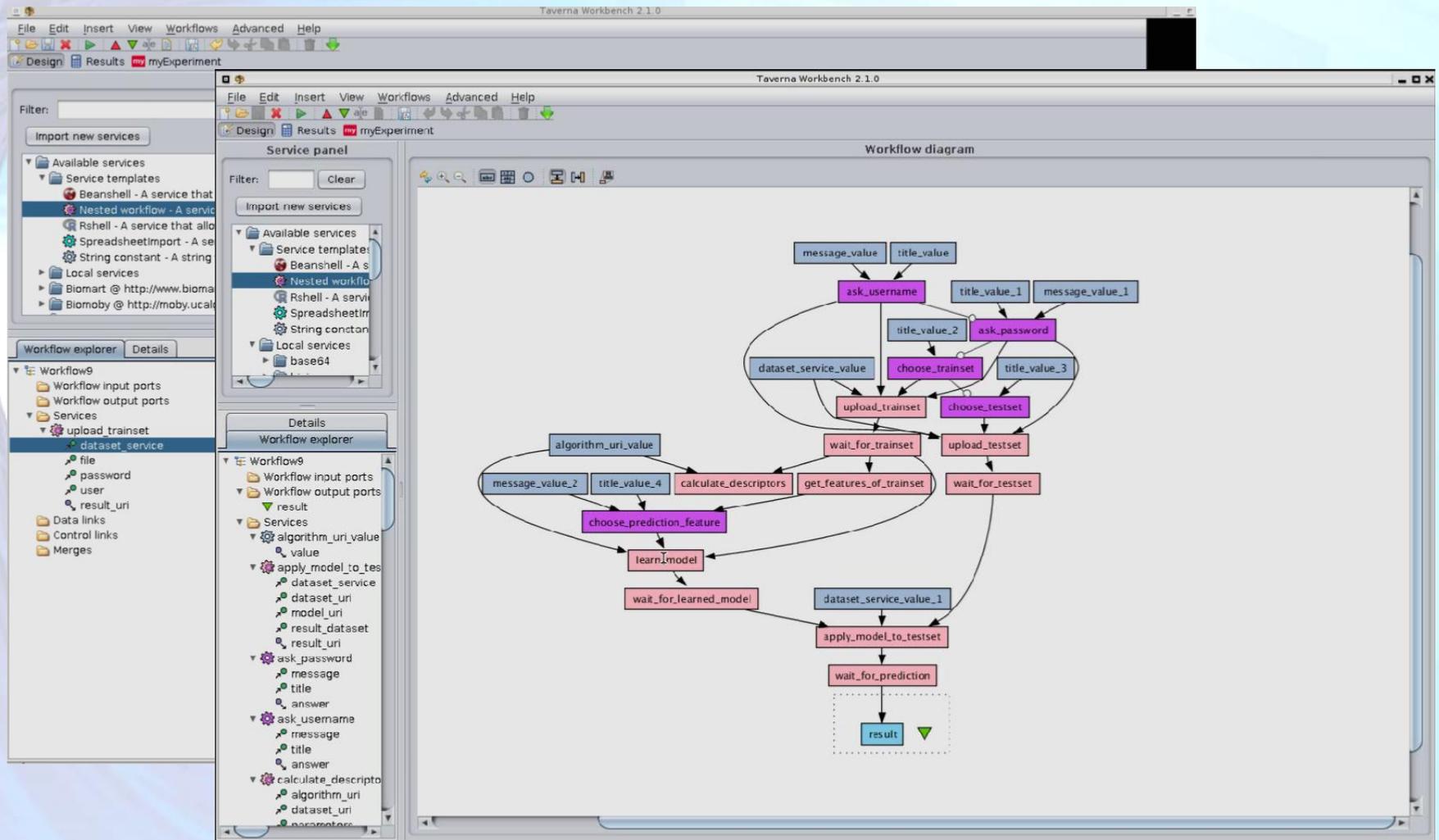
- OpenTox services can be integrated into workflows of tasks using workflow systems such as Taverna
- Supports the execution of multiple services in both synchronous and asynchronous tasks
- Goal is to support the integration of distributed chemical and biological data and modelling resources in more complex applications

Taverna Workflow System & OpenTox Services

The screenshot displays the Taverna Workbench 2.1.0 interface. The main window is divided into several panels:

- Service panel:** Located on the left, it contains a search filter, an "Import new services" button, and a list of available services. The "Nested workflow" service is currently selected.
- Workflow explorer:** Located below the service panel, it shows a tree view of the workflow structure, including "Workflow9", "Workflow input ports", "Workflow output ports", "Services", and "upload_trainset". The "dataset_service" is expanded to show its input ports: "file", "password", "user", and "result_uri".
- Input dialog:** A small dialog box is open in the center, titled "Input", with a question mark icon. It prompts the user to "Enter string value" and has the text "8080/ambit2/dataset/291/features" entered in the input field. "Cancel" and "OK" buttons are visible.
- Workflow diagram:** Located on the right, it shows a diagram of the workflow. It includes a "dataset_service" box with four output arrows pointing to "password", "user", and "file" boxes. These three boxes have arrows pointing to a "query_server" box. The "query_server" box has an arrow pointing to a "result_uri" box.

Taverna Workflow System & OpenTox Services

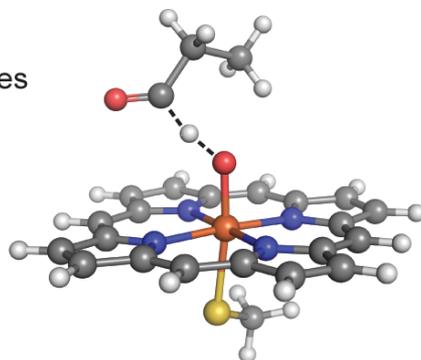


SMARTCyp Service for Predicting Metabolites

Atom Reactivity Library

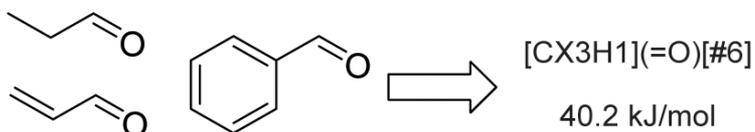
A. Calculate Quantum Chemical Reference Energies

Calculate transition state energies using density functional theory



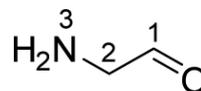
B. Define SMARTS Rules

Group calculations by fragments and calculate average energies



SMARTCyp

1. Assign Energies By SMARTS matching



Atom	SMARTS	Energy
1	[CX3H1](=O)[#6]	40.2
2	[CX4][N]	39.8
3	[N^3][H1,H2]	54.1

2. Compute Accessibility Descriptor

$$A_i = \text{Maxbonds}_i / \text{Maxbonds}_{\text{all}}$$



3. Compute Score and Rank Atoms

Score, $S = E - 8A$
Lowest score gets rank 1

$$S_1 = 40.2 - 8 \cdot 0.67 = 34.84$$

$$S_2 = 39.8 - 8 \cdot 0.67 = 34.44$$

$$S_3 = 54.1 - 8 \cdot 1.00 = 46.10$$

Atom 1 - Rank 2

Atom 2 - Rank 1

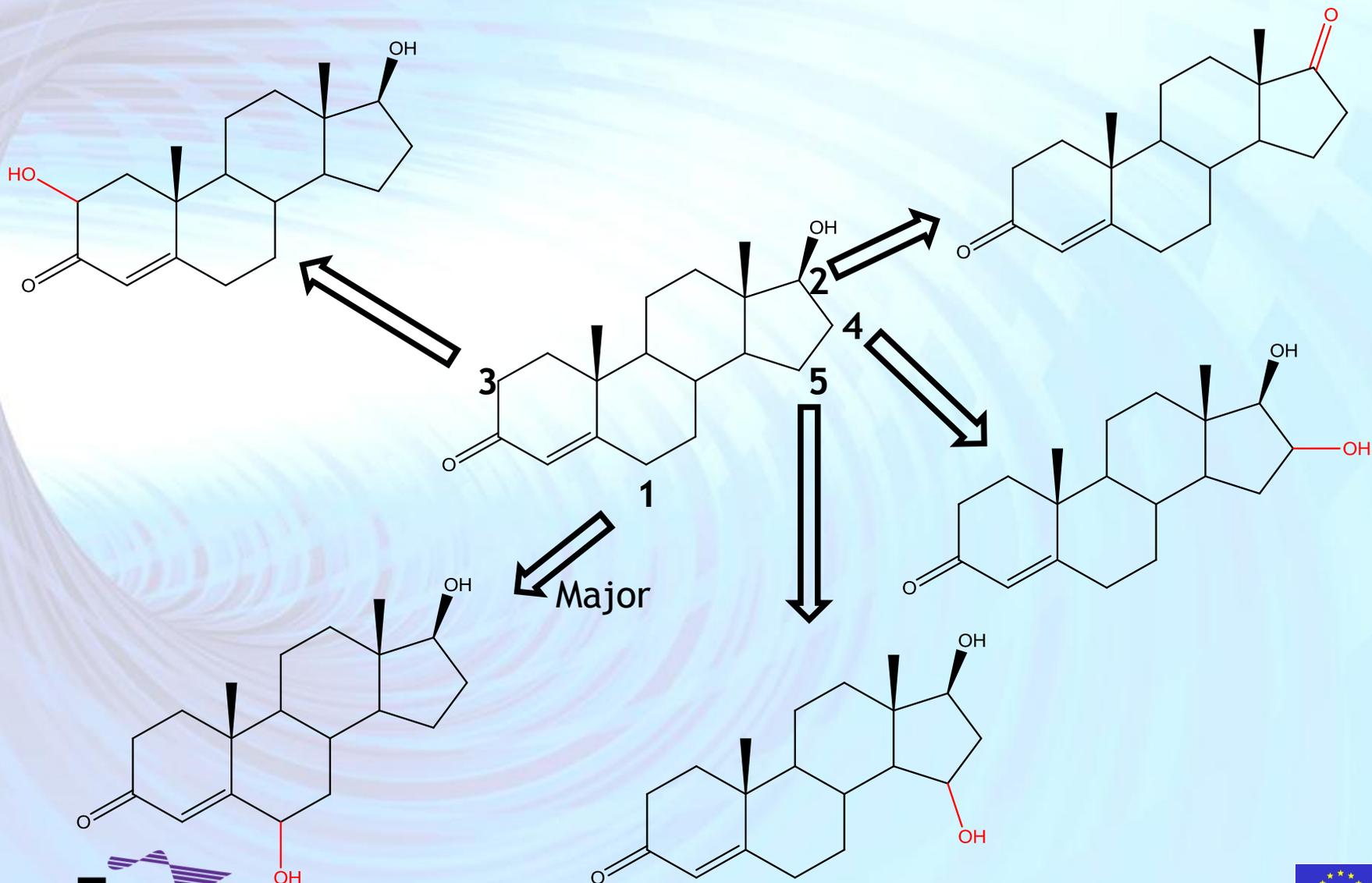
Atom 3 - Rank 3



SMARTCyp - developed by Patrik Rydberg, University of Copenhagen

www.farma.ku.dk/index.php/SMARTCyp/7990/0/

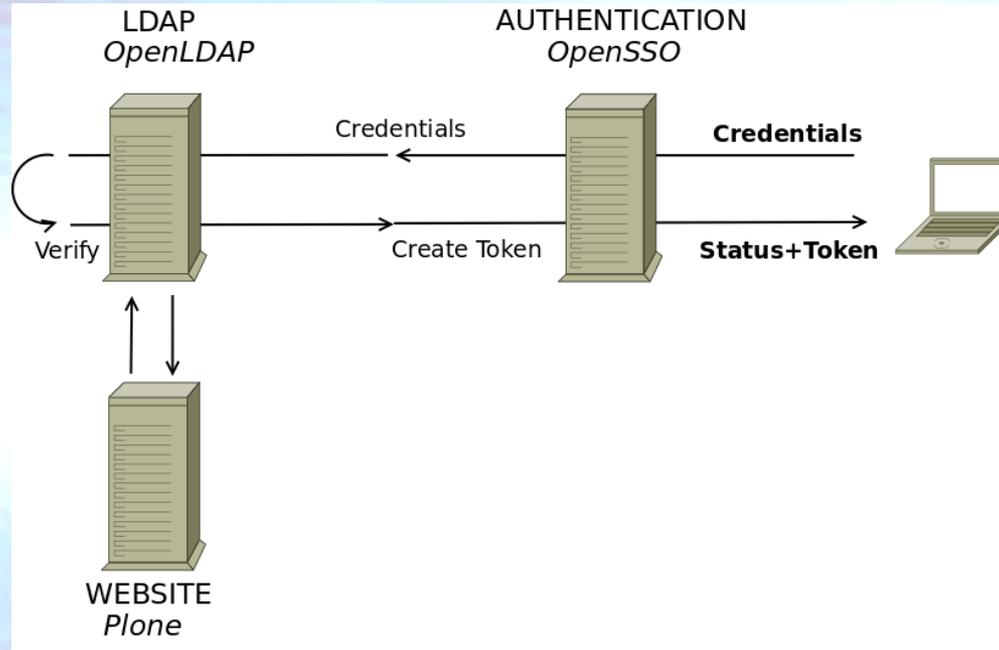
SmartCYP Prediction of Testosterone Metabolites



Controlling Access to Confidential Information

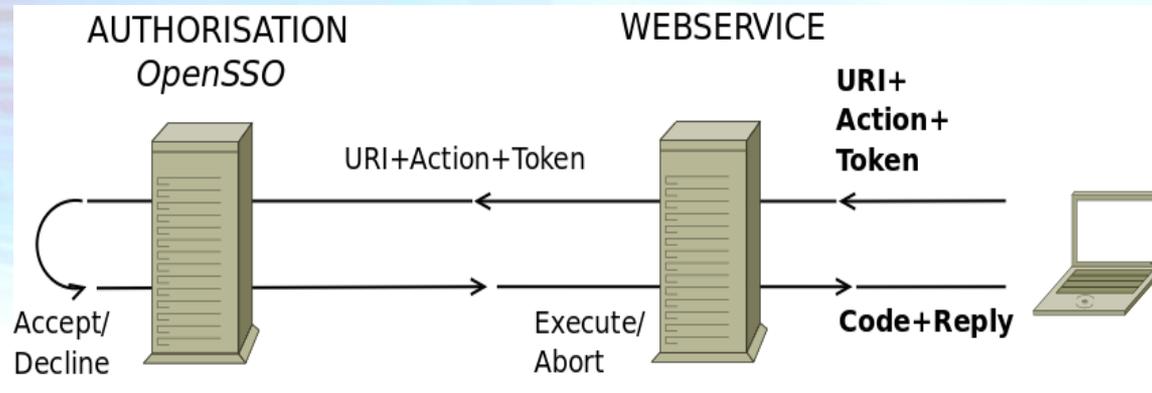
- OpenTox makes resources available through **URIs**
- OpenTox provides facilities to protect confidential information located at **URIs**. Two tasks are involved here:
 - **Authentication**: Confirming the identity of the user requesting access
 - **Authorisation**: Granting the confirmed identity access according to a set of restrictions described in policies

Authentication



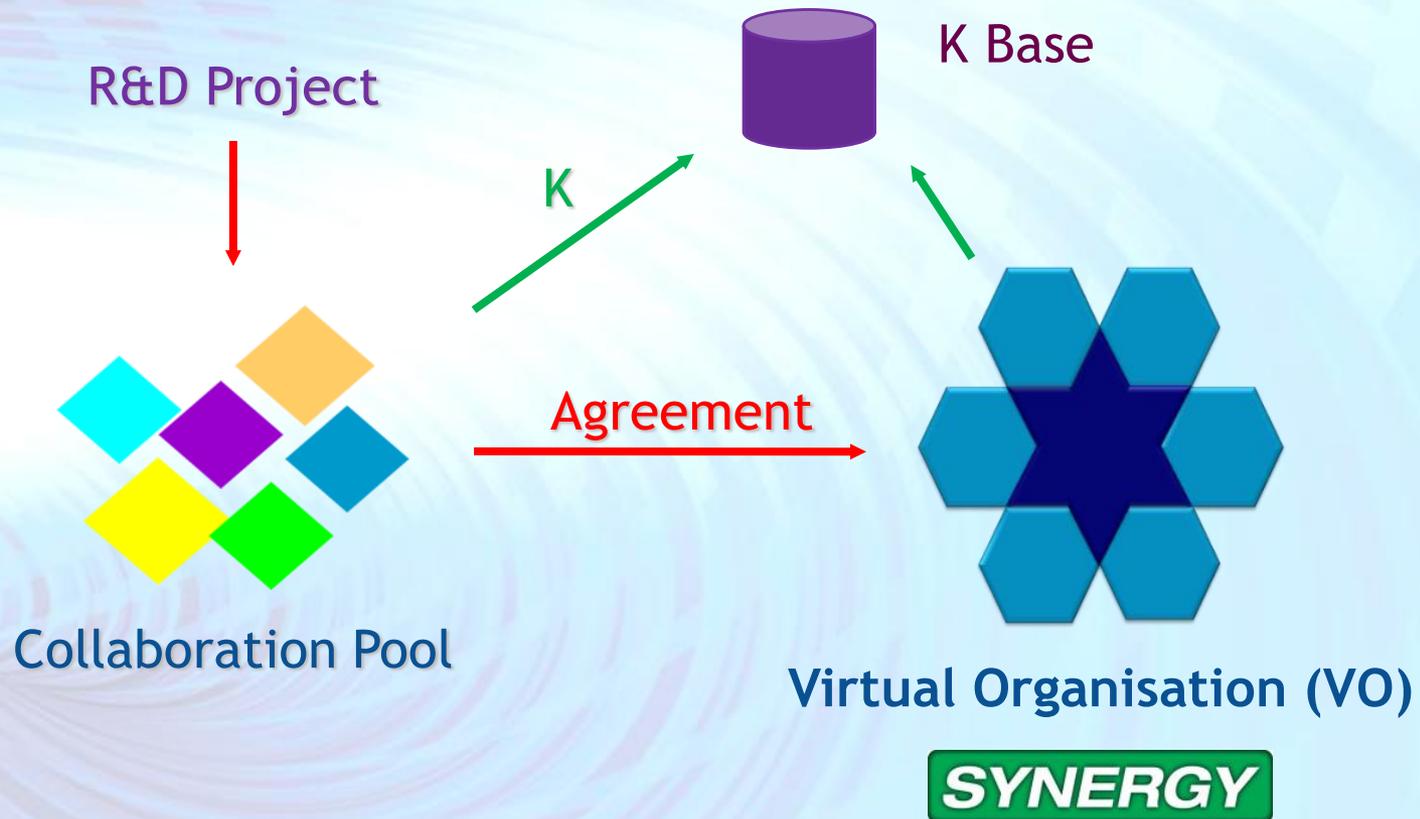
- Registered users are instantly available as potential users of OpenTox web services
- Users receive a token upon service request

Authorisation



- Tokens encode user identity
- Tokens are valid for a certain time period only (customizable)
- The triplet URI+Action+Token makes up the call to be authorised
- All messages are encrypted (SSL)
- Resource Owners create and modify policies defining access rules

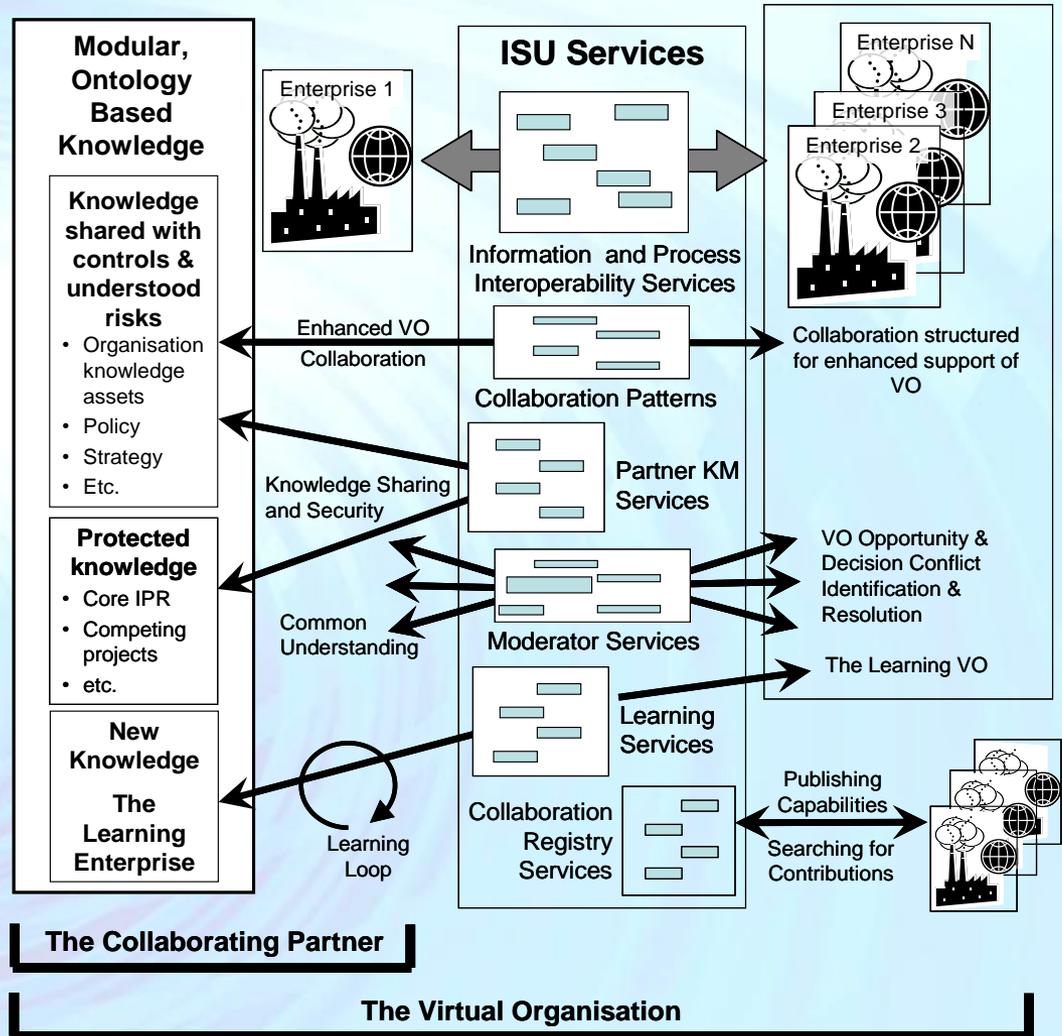
Virtual Organisation Pilots



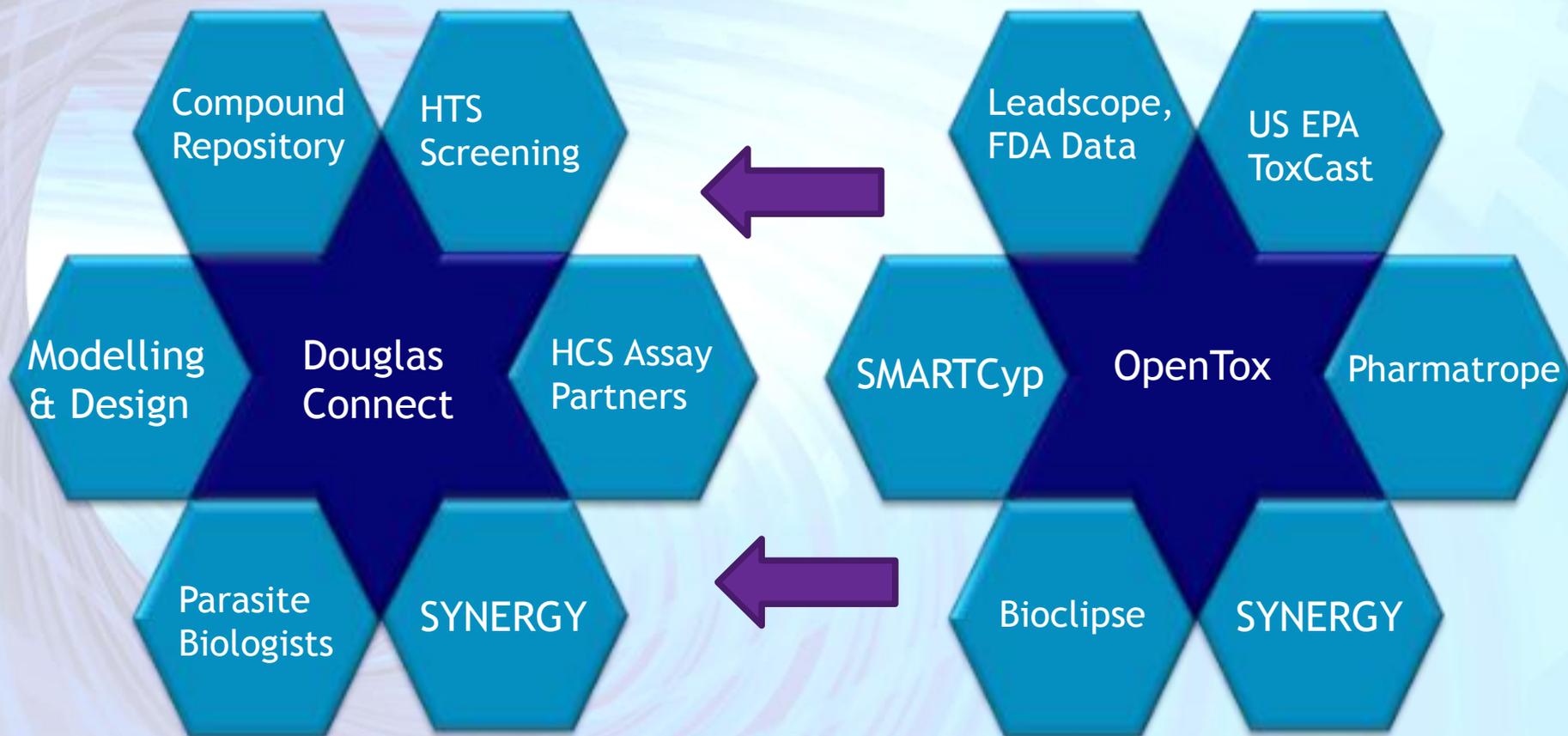
SYNERGY Collaboration Services for VOs



SYNERGY website:
www.synergy-ist.eu/



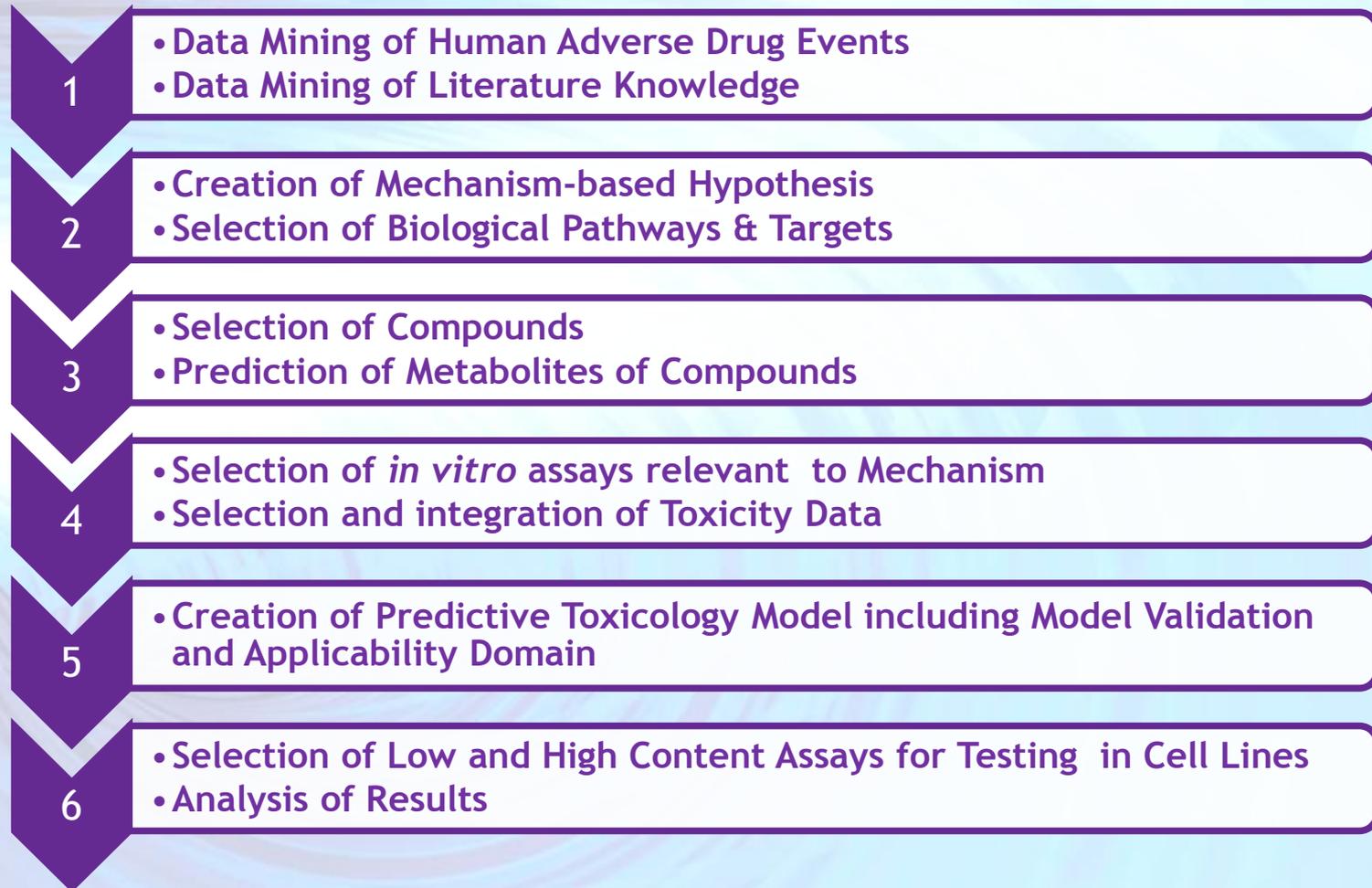
Virtual Organisation Pilots



Neglected Disease Drug Design VO

Predictive Toxicology VO

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



Recording of Collaborative R&D

Controlled Vocabularies

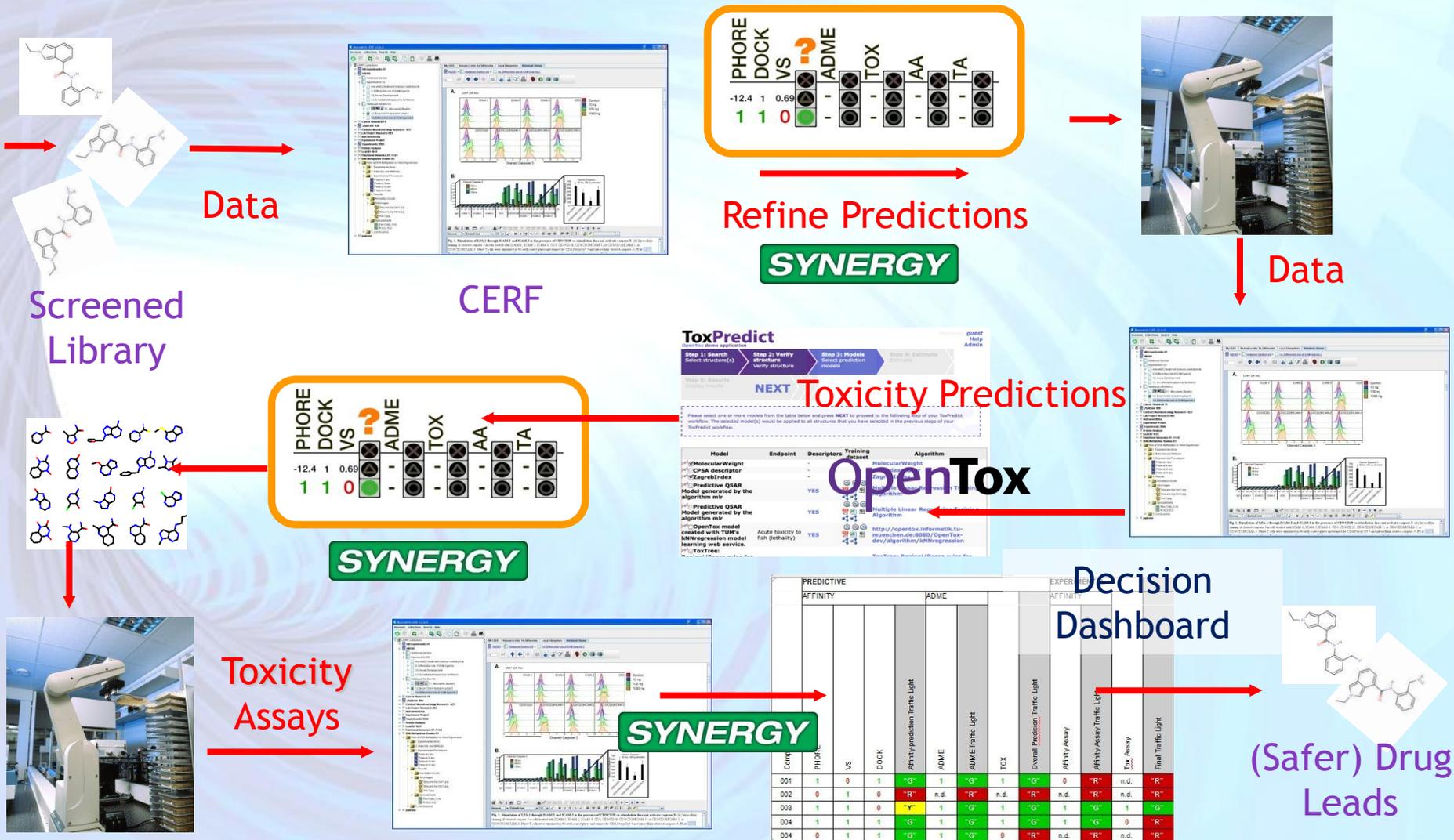
Visualisation

Collaborative Electronic Laboratory Notebook (ELN)

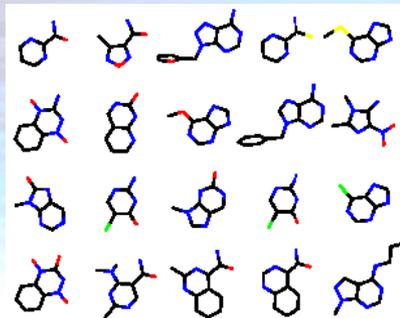
Fig. 1. Stimulation of LFA-1 through ICAM-2 and ICAM-3 in the presence of CD3/CD28 co-stimulation does not activate caspase-3. (A) Intracellular staining of cleaved-caspase 3 in cells treated with ICAM-1, ICAM-2, ICAM-3, CD3, CD3/CD28, CD3/CD28/ICAM-1, or CD3/CD28/ICAM-2, or CD3/CD28/ICAM-3. Naive T cells were stimulated in 96-well coated plates and stained for CD4-PerCPy5.5 and intracellular cleaved-caspase-3-FE at 24 hrs.

Condition	24 hrs	48 hrs	72 hrs
CD3/CD28	~550	~550	~550
CD3/CD28/ICAM-1	~350	~350	~350
CD3/CD28/ICAM-2	~150	~150	~150
CD3/CD28/ICAM-3	~450	~450	~450

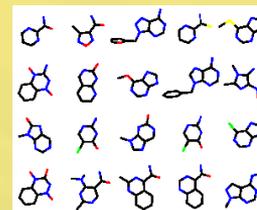
Synergy Collaboration Pilots



1. A library of compounds is entered to the ELN



ELN

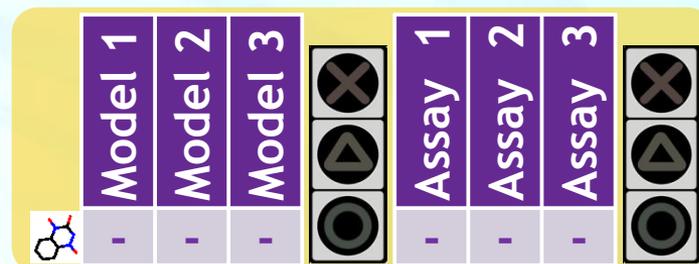


Synergy

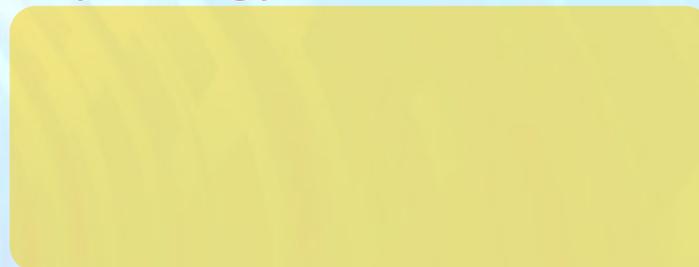
OpenTox

2. Each compound is assigned a data structure in ELN

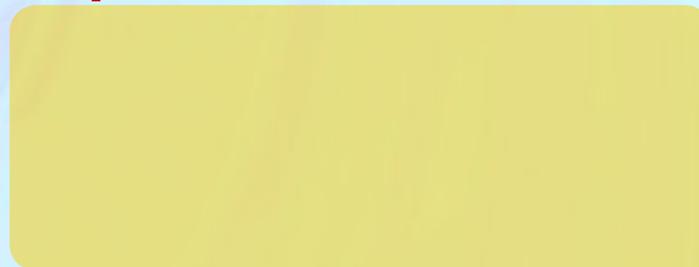
ELN



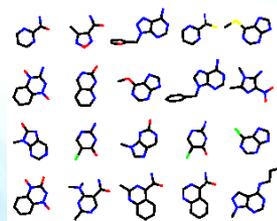
Synergy



OpenTox



3. ELN passes compounds to OpenTox and SYNERGY



ELN

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

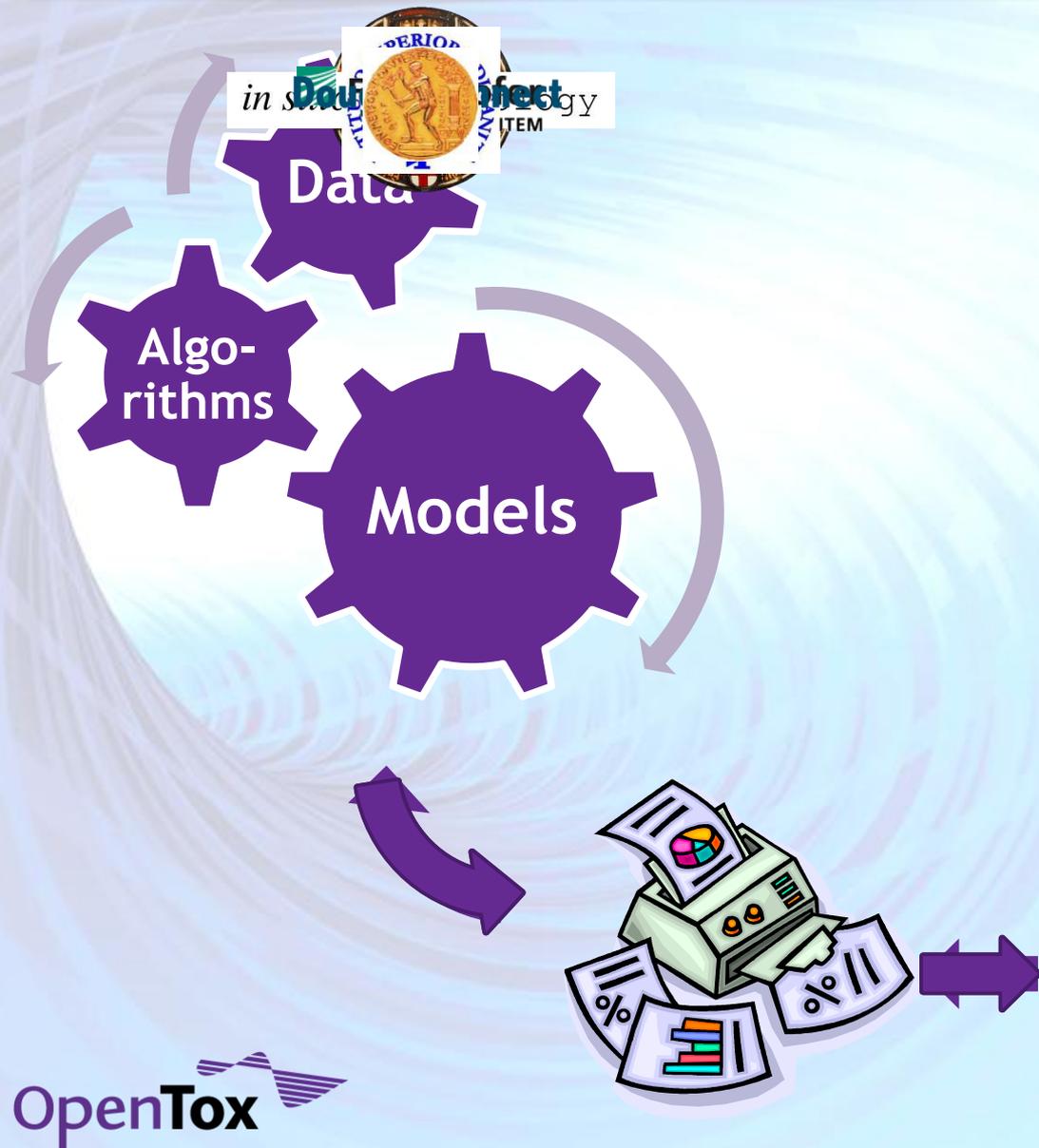
Synergy

	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		
-	-	-	-	-	-	-	-	-	-	-

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		-	-	-	

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		-	-	-	

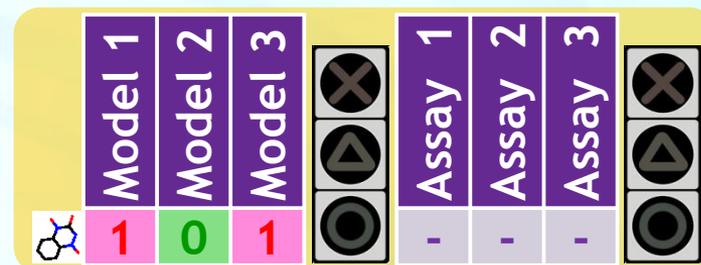
6. ELN sends the results to SYNERGY



7. SYNERGY applies the Recommendation Rules



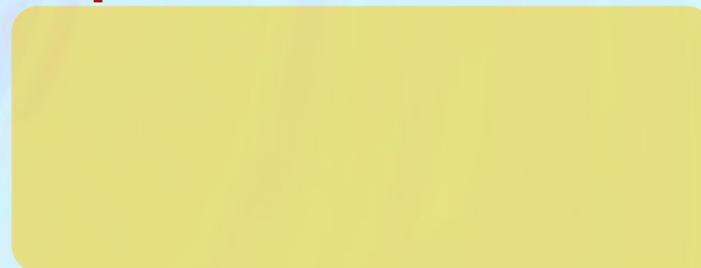
ELN



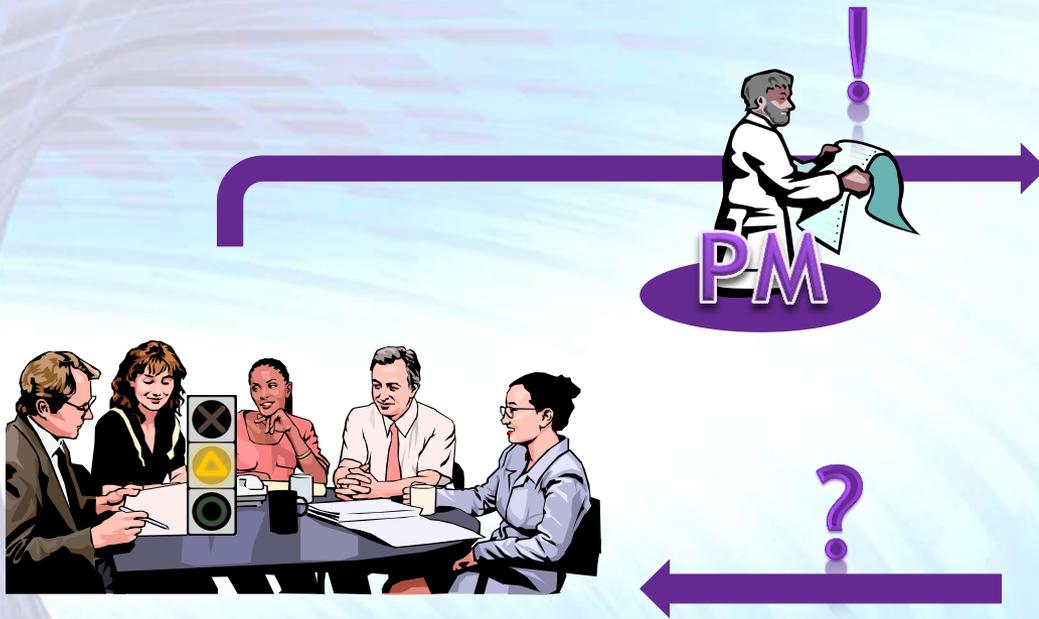
Synergy



OpenTox



8. Inconclusive data → SYNERGY calls a meeting



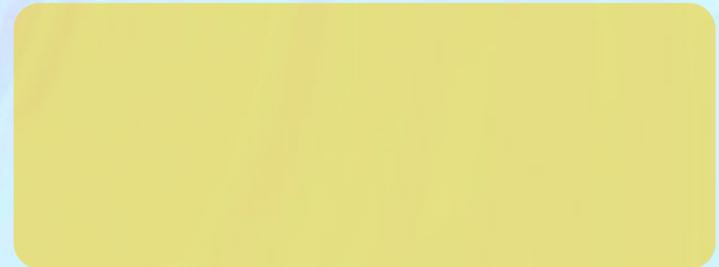
ELN

	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		-	-	-	

OpenTox



9. Experimental assays confirm toxicity



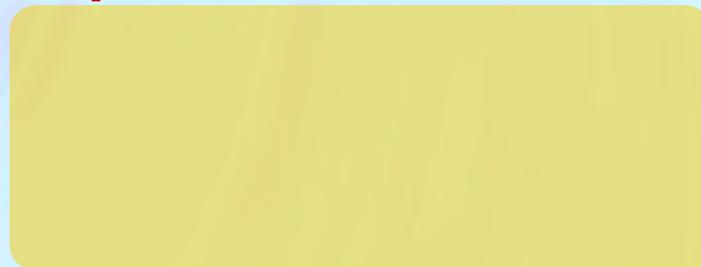
ELN

	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		-	-	-	
								
								

OpenTox



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OpenTox Advisory Board

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- LHASA
- Leadscope
- University of North Carolina
- EC Environment Directorate General
- Organisation for Economic Cooperation & Development
- CADASTER
- Bayer Healthcare

Final words...

For more information, visit

www.opentox.org

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**Many thanks for your
attention!**

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