

Directions for Integrated Analysis in Predictive Toxicology (*that extend current strategies, methods and infrastructure to better include development and support of a combination of statistical, mechanistic and pathways based approaches to optimise progress in the quality and acceptance of alternative testing methods*)

Barry Hardy

**(OpenTox Coordinator &
Douglas Connect)**

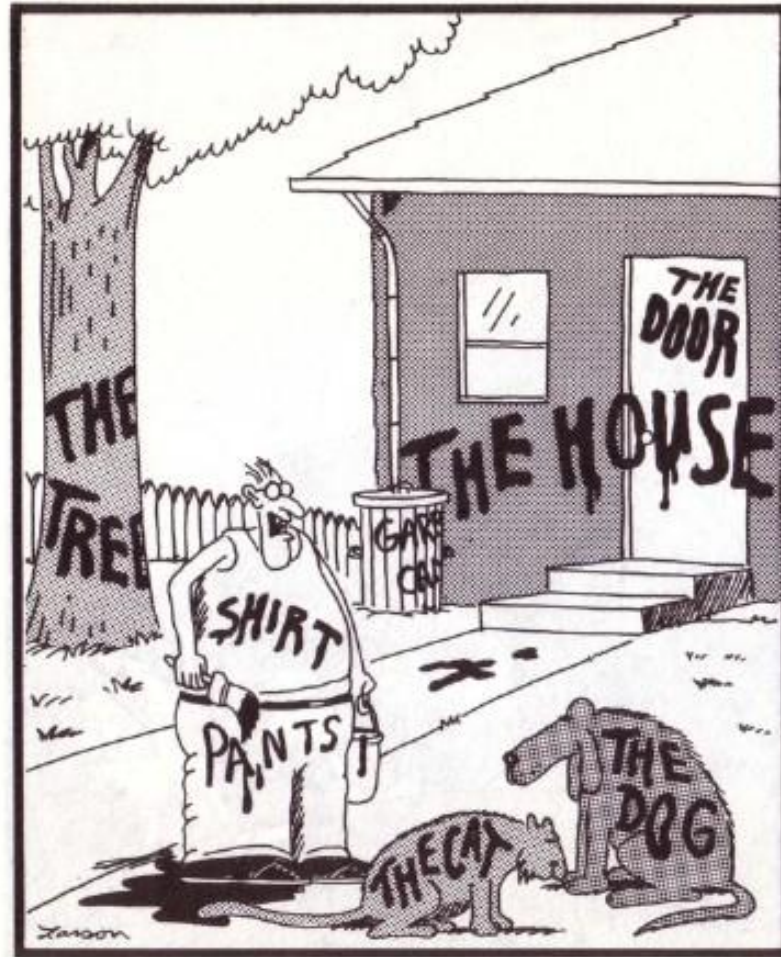
OpenTox Presentation

21 October 2010

PathProt III

IGC, Oeiras, Portugal

Semantic Reflections



"Now! ... That should clear up
a few things around here!"

Collaborating Partners

In Silico Toxicology,
Switzerland

Douglas Connect,
Switzerland

Albert Ludwigs University
Freiburg, Germany

Ideaconsult,
Bulgaria

Istituto Superiore
di Sanità, Italy

National Technical
University of Athens,
Greece

Fraunhofer Institute
for Toxicology &
Experimental Medicine,
Germany



Technical University
of Munich, Germany

David Gallagher, UK

Institute of Biomedical
Chemistry of the Russian
Academy of Medical
Sciences, Russia

Seascope Learning &
JNU, India

Summary

Part 1

Overview of the outcomes of the first two years of work in the development of the OpenTox Community and Framework for Predictive Toxicology. Concepts and implementations - what we have done so far...

... leading into **Part 2** discussions on future directions with regards to mechanism and pathways.

The OpenTox Framework as of early 2010 - see Journal of Cheminformatics Publication

Collaborative development of predictive toxicology applications
Journal of Cheminformatics 2010, 2:7 doi:10.1186/1758-2946-2-7

Barry Hardy, Nicki Douglas, Christoph Helma, Micha Rautenberg, Nina Jeliaskova, Vedrin Jeliaskov, Ivelina Nikolova, Romualdo Benigni, OlgaTcheremenskaia, Stefan Kramer, Tobias Girschick, Fabian Buchwald, JoergWicker, Andreas Karwath, Martin Gutlein, Andreas Maunz, Haralambos Sarimveis, Georgia Melagraki, Antreas Afantitis, Pantelis Sopasakis, David Gallagher, Vladimir Poroikov, Dmitry Filimonov, Alexey Zakharov, Alexey Lagunin, Tatyana Gloriovova, Sergey Novikov, Natalia Skvortsova, Dmitry Druzhilovsky, Sunil Chawla, Indira Ghosh, Surajit Ray, Hitesh Patel and Sylvia Escher

Open Access publication available at
www.jcheminf.com/content/2/1/7

Step 1: Search

Select structure(s)

Step 2: Verify structure

Verify structure

Step 3: Models

Select prediction models

Step 4: Estimate

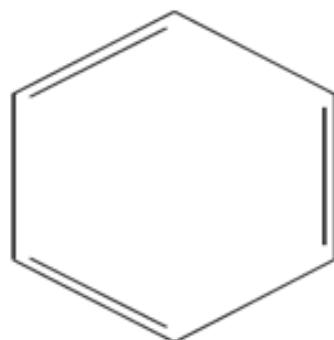
Estimate

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

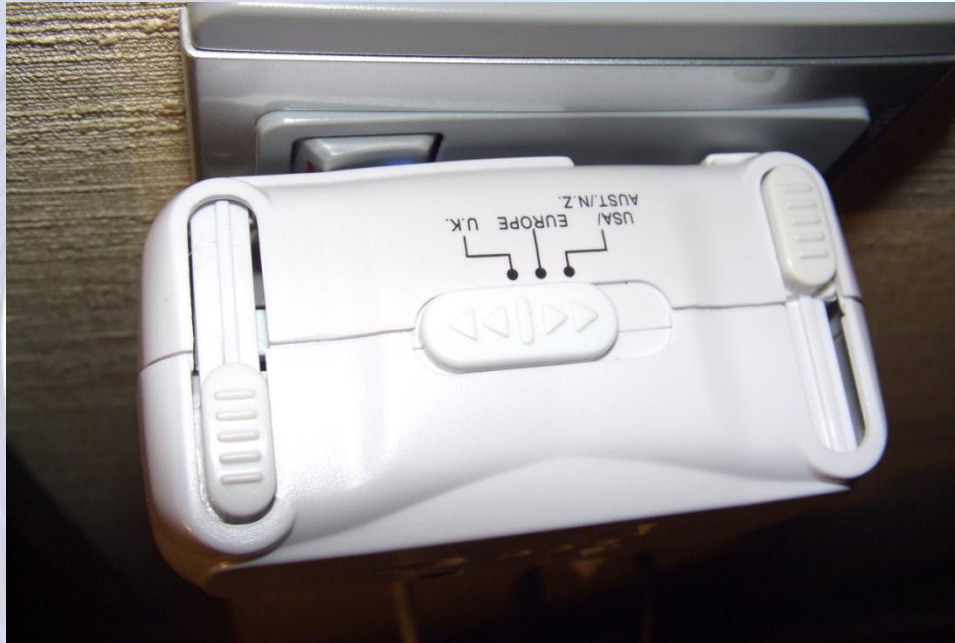
21742.0
Benzene
benzene
OK

MolecularWeight  **MolecularWeight**

MW

78.1112

Absence of Interoperability creates Problems



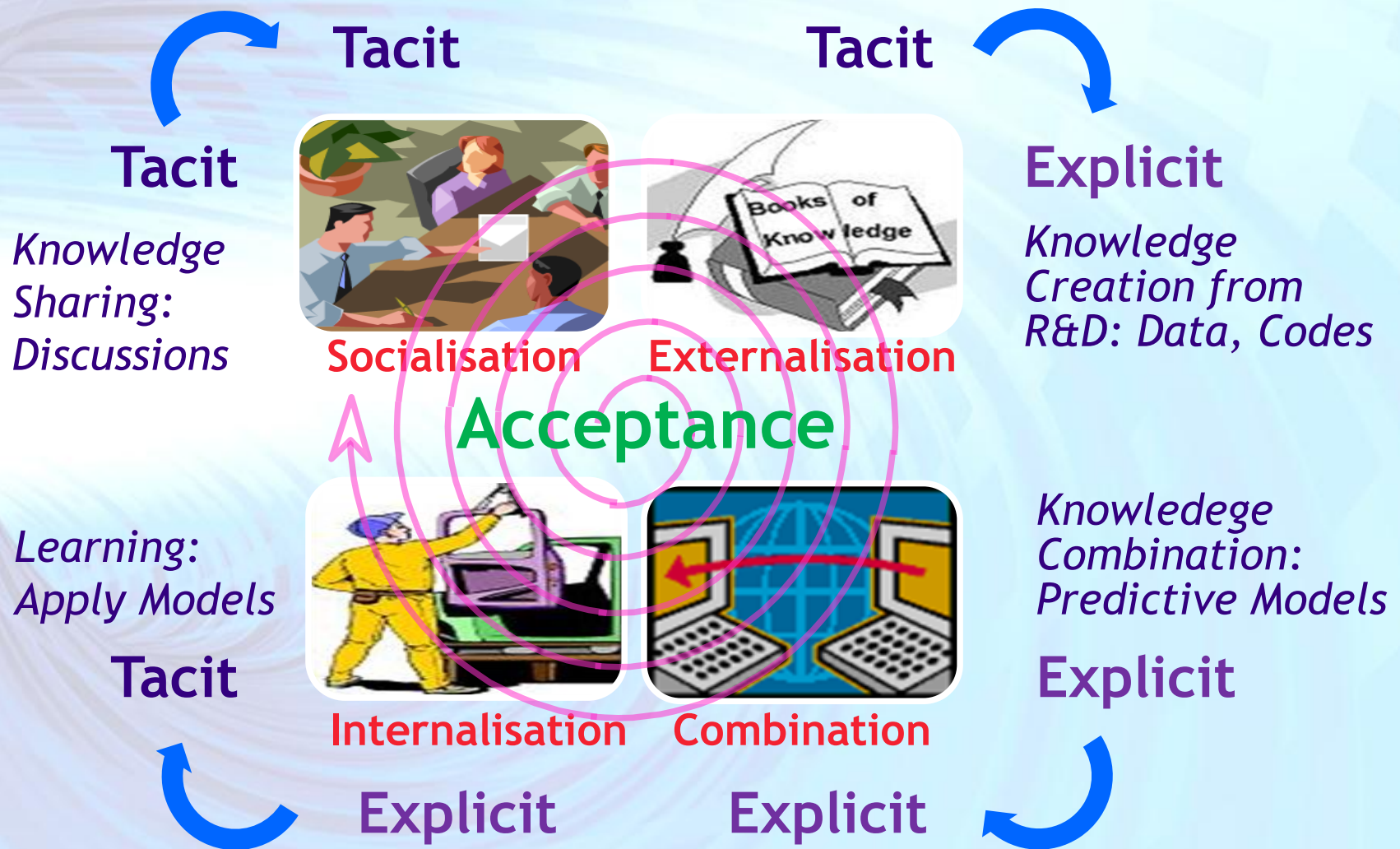
Adaptor Challenge in Jeddah, 2008

Interacting Components create Solutions



Adaptor Solution in Jeddah, 2008

SECI Model for Knowledge Management



Complexity Context

Non Repeatable
Adaptative, Patterns,
Filters

Sense
Making for
Emergent
Practice

Leadership
Novel
Practice

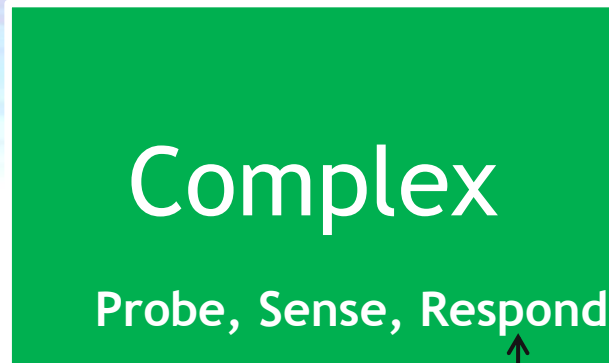
Lack of Cause & Effect, Stability-focused
Intervention, Crisis Management

Complex Cause & Effect
Systems Thinking, Analysis

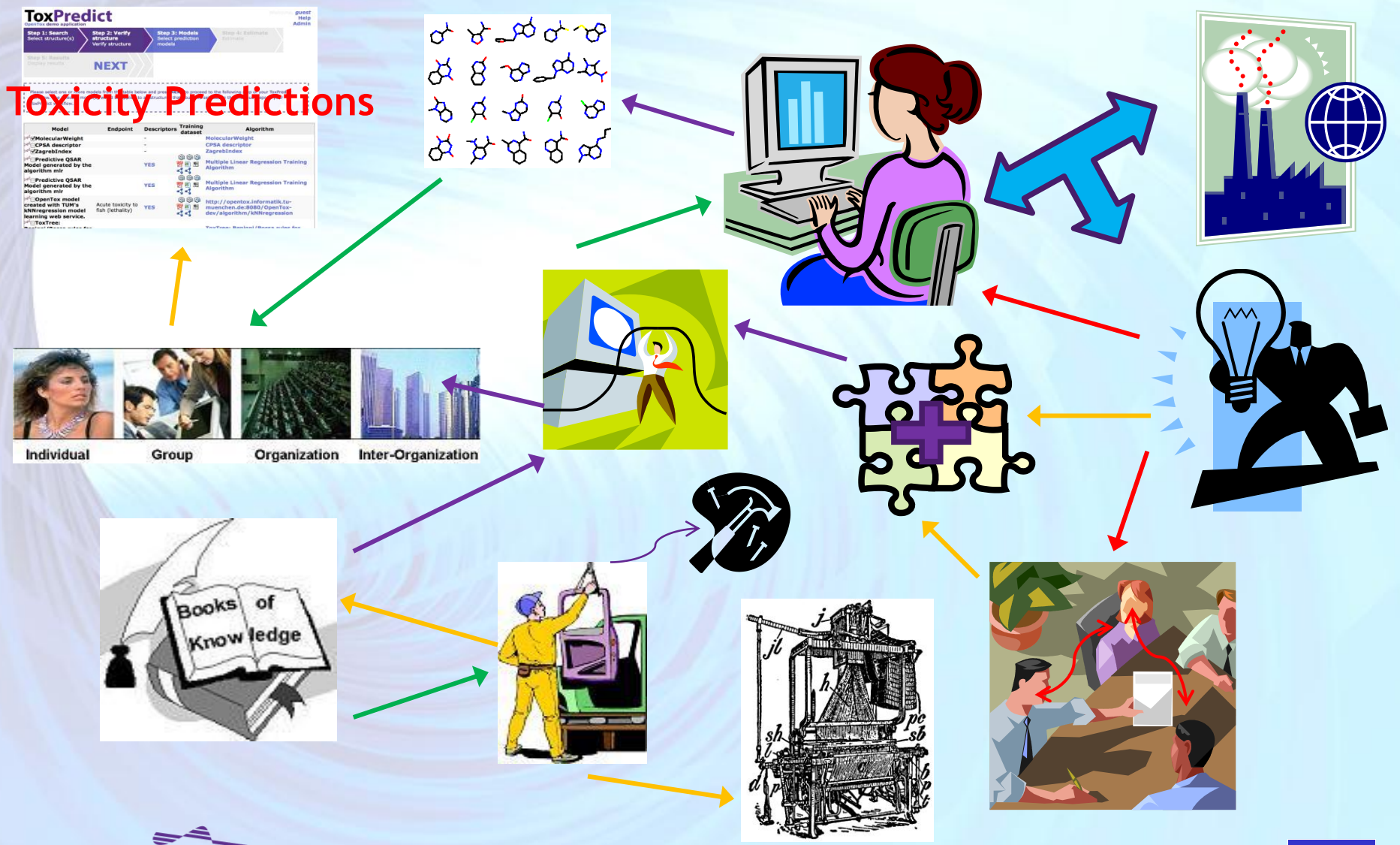
Processes
Good
Practice

Procedures
Best
Practice

Cause & Effect
Repeatable, SOPs



Accelerating Knowledge Flows in Predictive Toxicology



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:

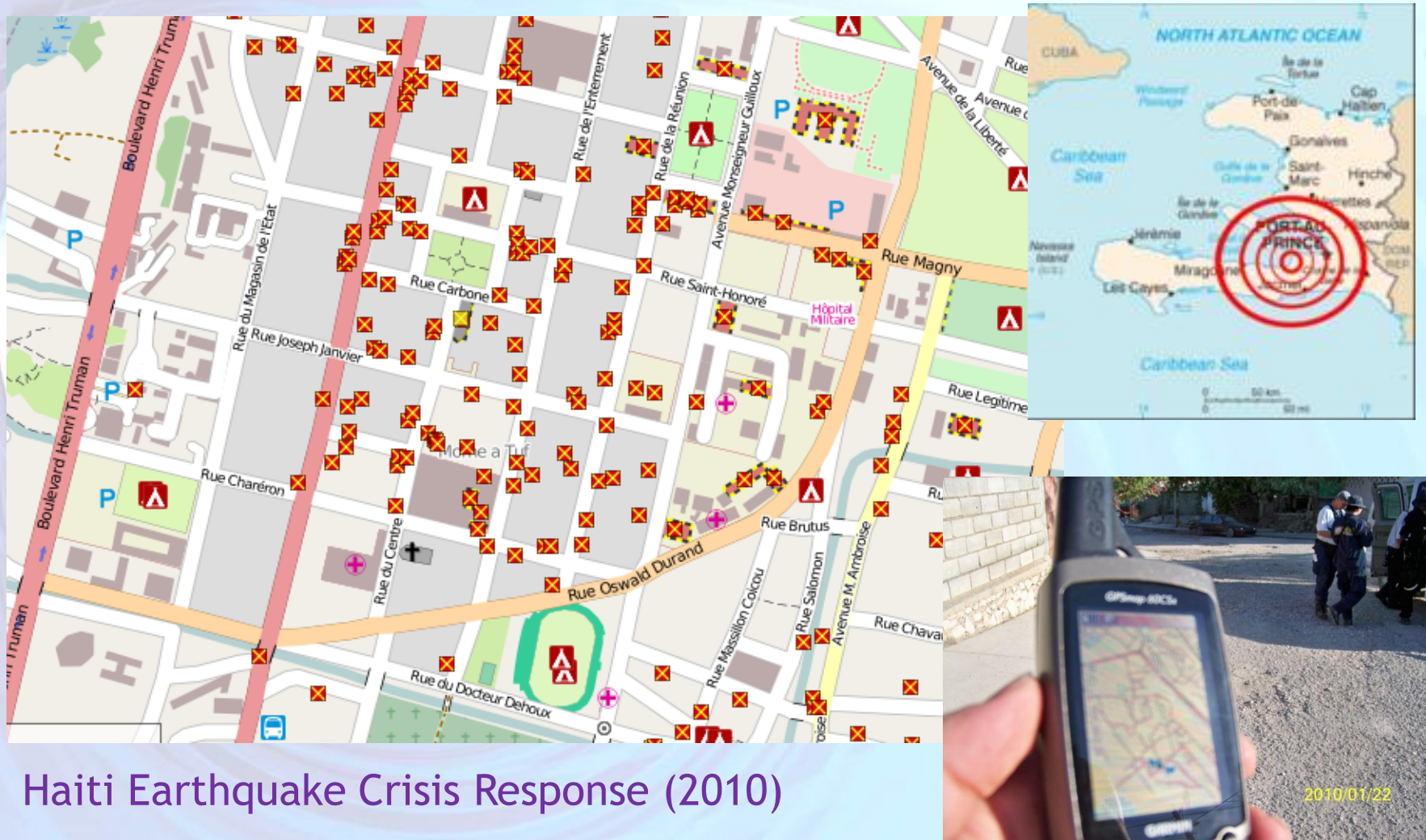
1. Provision of a **URI** that describes a Data Resource
2. Use of **HTTP** to retrieve useful data from the **URI**
3. A Data Format described with standardised semantics (so relationships are enabled) e.g. **RDF**
4. Data should provide links to other Data (through **URIs**)

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

Solution created by Linked Open Data, Web Applications and Crowdsourcing



Haiti Earthquake Crisis Response (2010)

wiki.openstreetmap.org

OpenTox is an Integrating Framework

A diagram on the left side of the slide consists of three concentric purple semi-circles. The outermost semi-circle is the largest, the middle one is smaller, and the innermost one is the smallest. These semi-circles are positioned to the left of a table, with their right edges aligned with the table's columns. The table has three rows, each corresponding to one of the semi-circles. The first row is associated with the largest semi-circle, the second with the middle one, and the third with the smallest one. The table's first column contains the labels 'Framework', 'Diverse Access', and 'Interoperability' respectively. The second column contains bulleted lists of details for each category.

Framework

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

Diverse Access

- Toxicolog, Biolog, 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

OpenTox Components

Compounds: Structures, names, ...

Features: Chemical and biological (toxicological) properties, substructures, ...

Datasets: Relationships between compounds and features

Algorithms: Instructions for solving problems

Models: Algorithms applied to data yield models which can be used for predictions

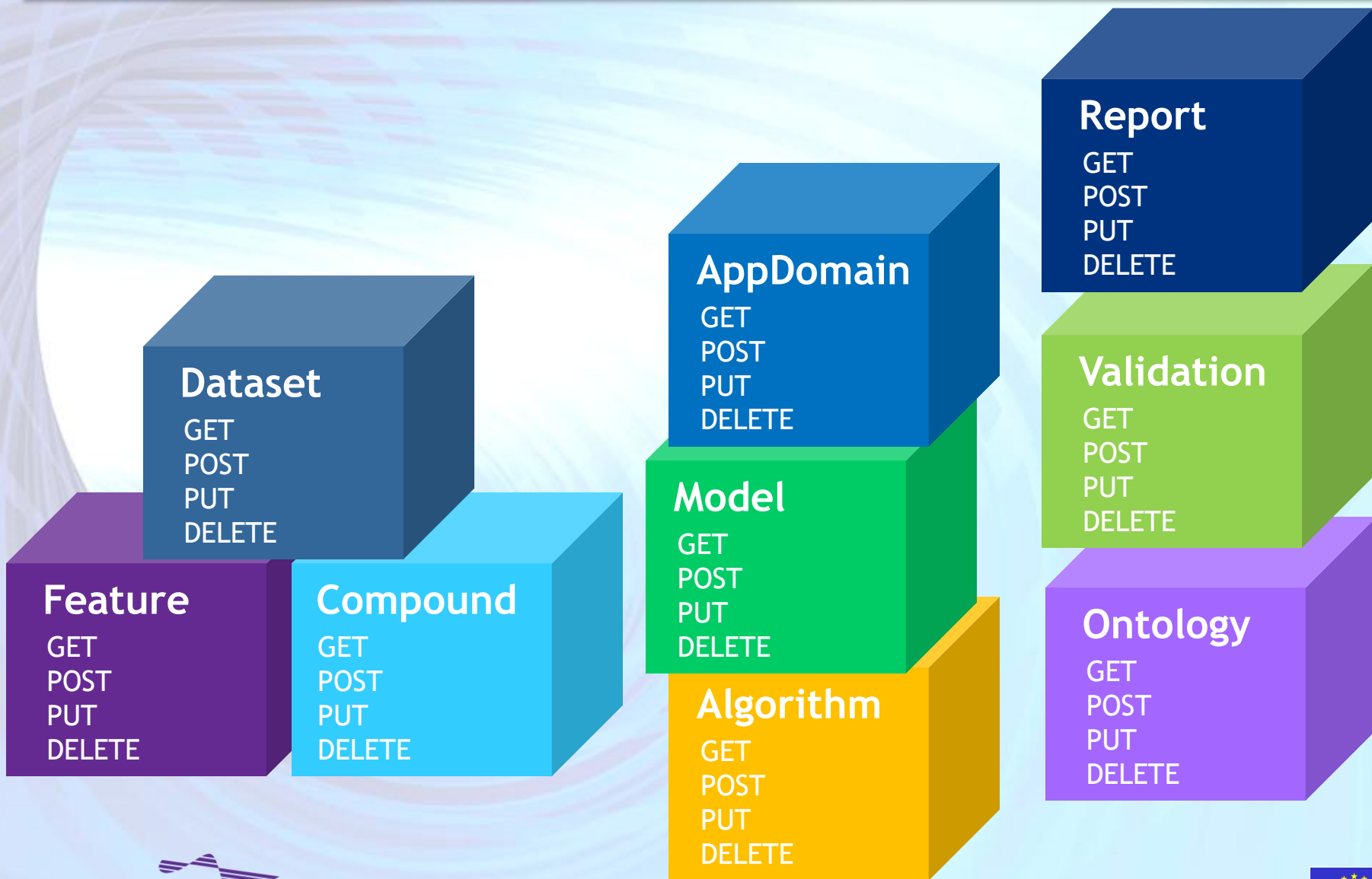
Validation: Methods for estimating the accuracy of model predictions

Reports: Report predictions and models e.g. to regulatory authorities

Tasks: Handle long running calculations

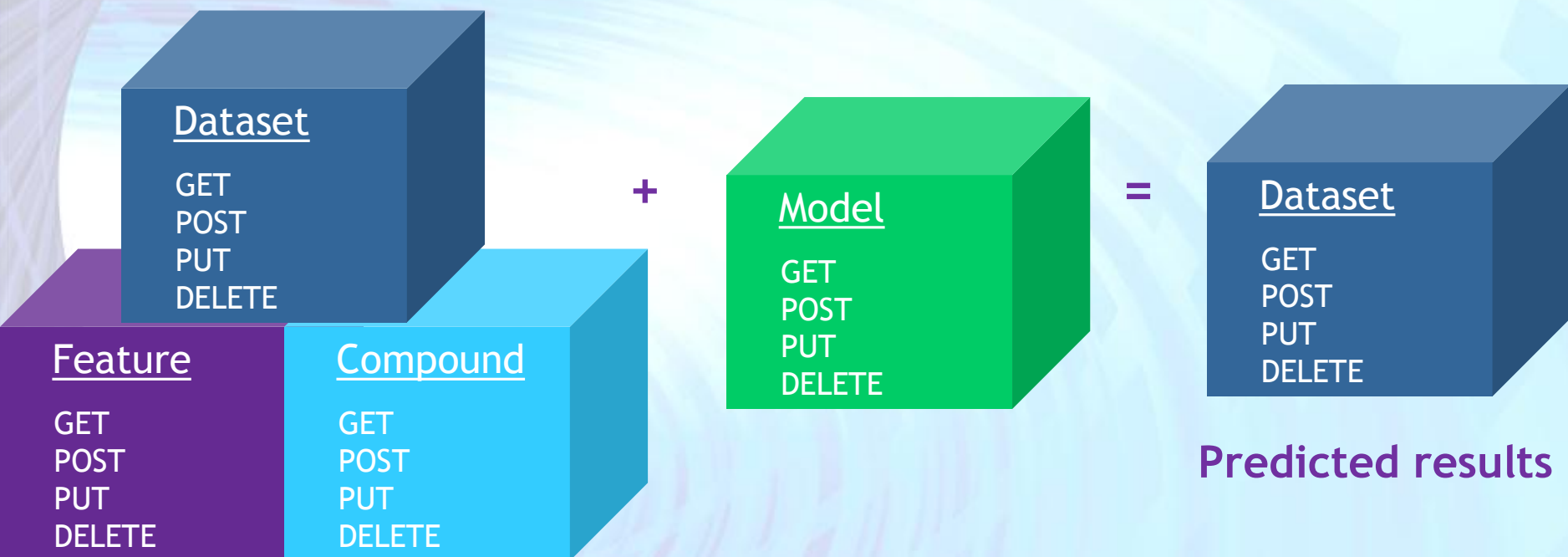
Authentication and Authorisation: Protect confidential data

Overview of Application Programming Interfaces



Uniform access to calculations

Read data from a web address - process - write to a web address



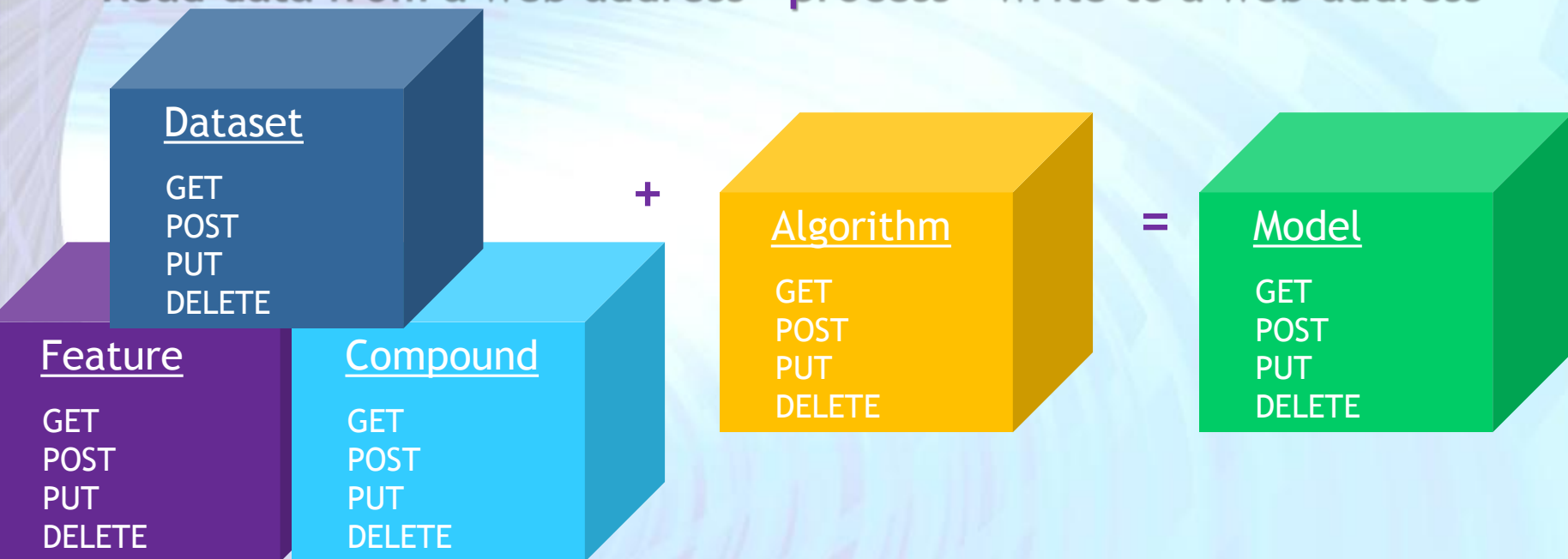
<http://myhost.com/dataset/newcompounds>

<http://myhost.com/model/predictivemodel1>

<http://myhost.com/dataset/predictedresults1>

Uniform approach to models creation

Read data from a web address - process - write to a web address



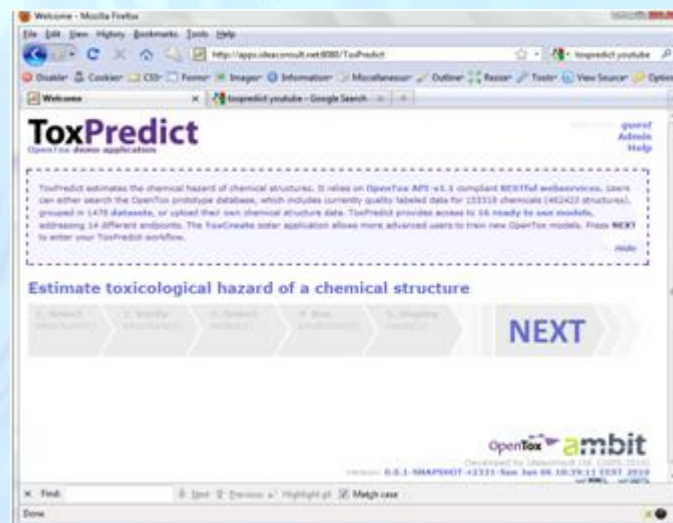
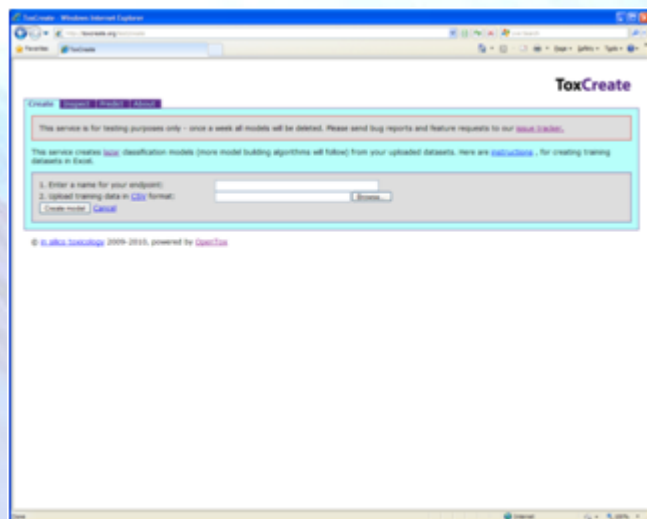
<http://myhost.com/algorithm/neuralnetwork>

<http://myhost.com/dataset/trainingset1>

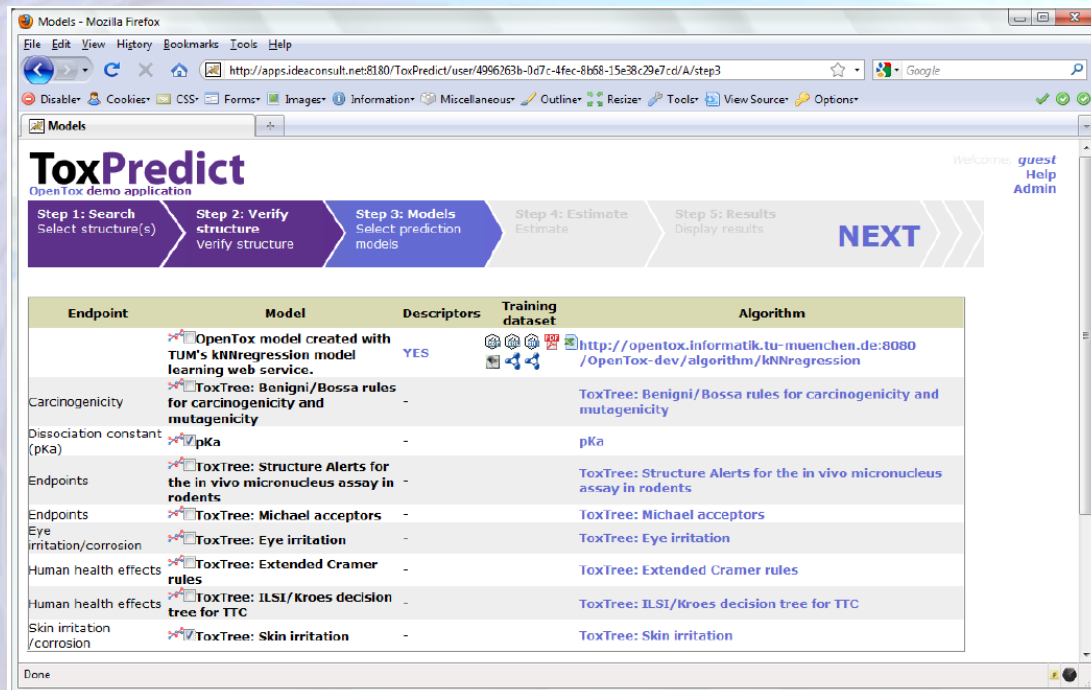
<http://myhost.com/model/predictivemodel1>

Prototype applications

- Two end user oriented demo applications, making use of OpenTox webservices, have been developed, deployed and are available for testing - toxcreate.org and toxpredict.org
- ToxCreat creates models from user supplied datasets
- ToxPredict uses existing OpenTox models to estimate chemical compound properties



What you can do with it ...



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

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

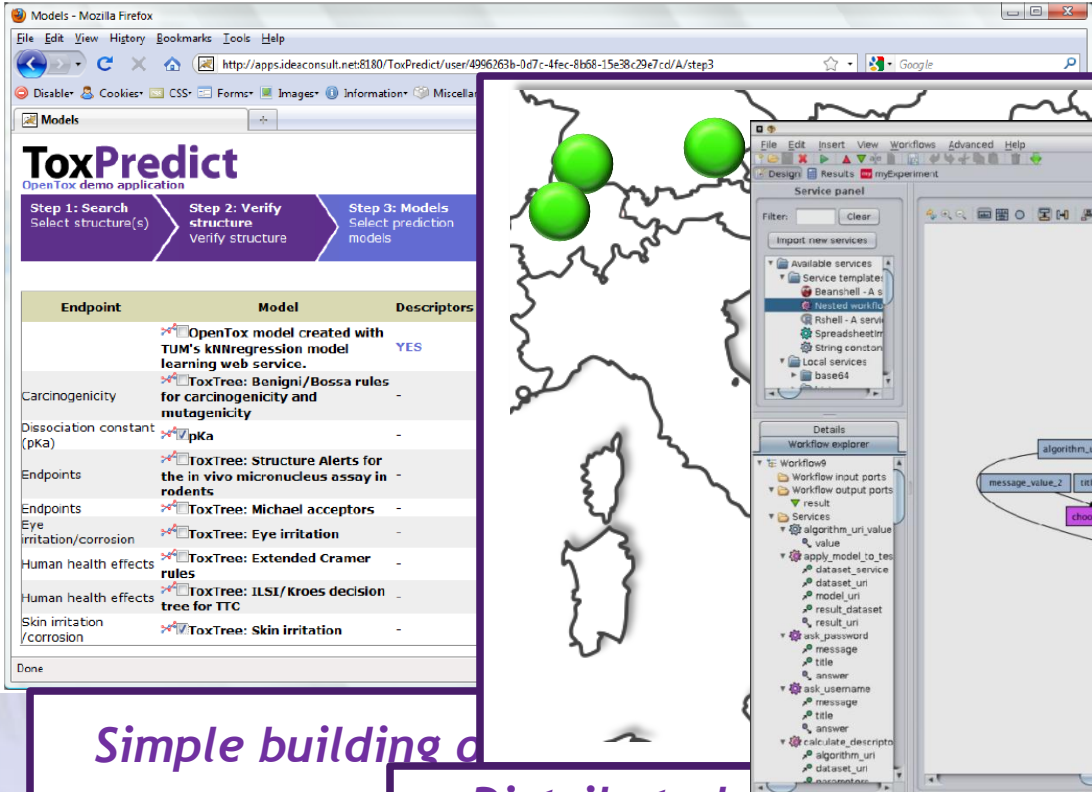
Endpoint	Model	Descriptors
	OpenTox model created with TUM's kNNregression model learning web service.	YES
Carcinogenicity	ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	-
Dissociation constant (pKa)	pKa	-
Endpoints	ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents	-
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	-

Below the table is a 'Done' button. To the right of the browser window is a map of Europe with five green circular markers placed in various locations: two in Northern Europe (UK/Ireland area), one in Central Europe (Germany area), and two in Southern Europe (Spain/Italy area).

Simple building of applications methods and

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

What you can do with it ...



The screenshot shows the ToxPredict web application interface. It includes a navigation bar with three steps: Step 1: Search, Step 2: Verify, and Step 3: Models. Below this is a table with columns for Endpoint, Model, and Descriptors. The table lists various models and their associated endpoints and descriptors.

Endpoint	Model	Descriptors
Carcinogenicity	OpenTox model created with TUM's kNN regression model learning web service.	YES
Dissociation constant (pKa)	ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	-
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	-

Simple building of applications

Distributed of wide range of methods

Integration into workflow systems for computational biology

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)[C@H](O)[C@H](O)[C@H](O)[C@H](O)[C@H](O)C1CCCC1

Chemical compounds

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

ambit

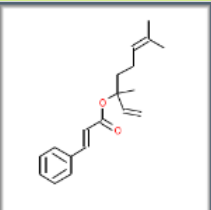
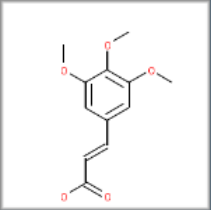
SMARTS Draw substructure

Keywords Search

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

Retrieve data

Search results SMARTS [*]OC(=O)[C@H](O)[C@H](O)[C@H](O)[C@H](O)[C@H](O)C1CCCC1 Download as Max number of hits: 100

#	Compound	ECHA REGISTRATION DATE	ECHA CasRN	ECHA EC	ECHA Names	ECHA SYNON Names	ECHA SYNON Names	ECHA SYNON Names	ECHA SYNON Names	ECHA SYNON Names	ECHA SYNON Names
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						

http://apps.ideaconsult.net

Interoperability & Vocabulary

Dogs

- Collie
- Labrador



Cats

- Siamese
- Persian



Birds

- Sparrow
- Owl



Interoperability & Vocabulary



Interoperability & Ontology

Org A

Collie

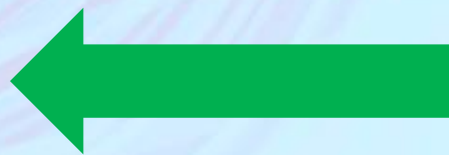


Siamese



Org B

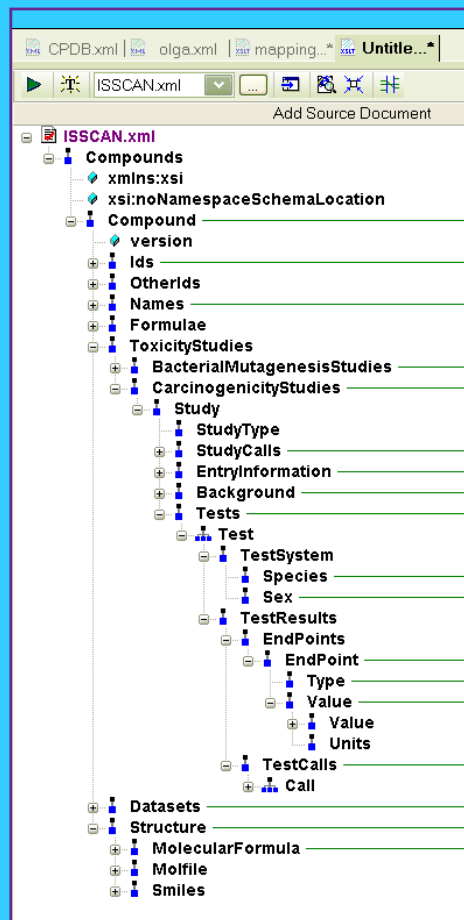
Collie



Siamese

Toxicological Endpoint Ontology Development

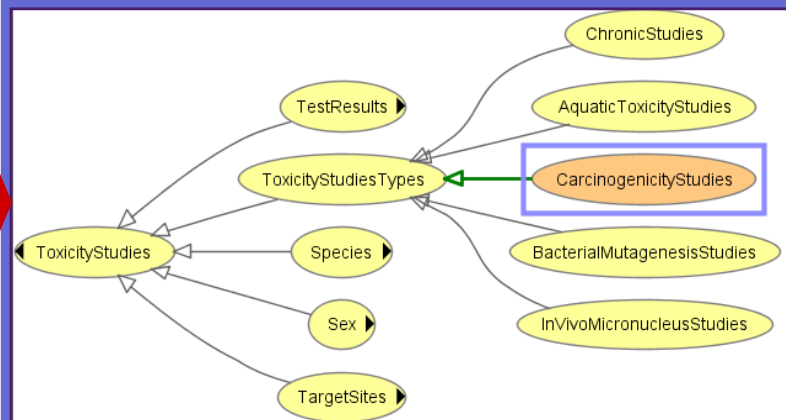
ToxML schema



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

OpenTox Toxicological Endpoint Ontology

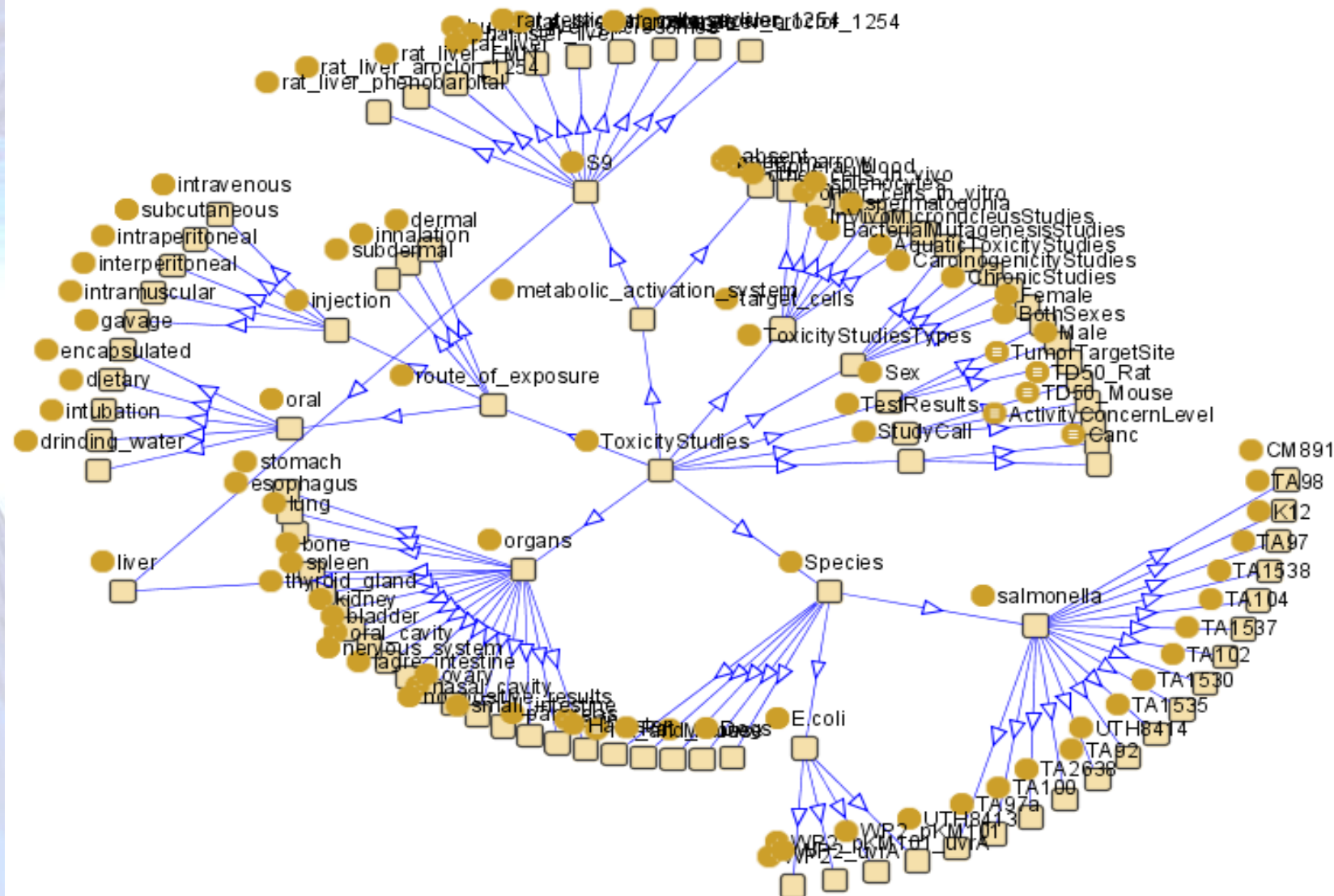
Ontology Development



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

Collaborative
Protégé
Environment

Toxicological Ontology: graphical representation



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

OpenToxipedia



Barry Hardy Log out Quicktools Site Setup Help

Site Map Accessibility Contact Data

Search Site

Home Toxicity Prediction OpenTox Blog People Partners Development OpenToxipedia
User Guidance Latest Entries A B C D E F G H I J K L M N O P Q R S T U V W
X Y Z by Categories Entries OpenToxipedia

You are here: Home » OpenToxipedia

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



Dataset and Ontology - find an assay, linked to specific gene

```
PREFIX ot:<http://www.opentox.org/api/1.1#>
PREFIX ota:<http://www.opentox.org/algorithms.owl#>
PREFIX owl:<http://www.w3.org/2002/07/owl#>
PREFIX dc:<http://purl.org/dc/elements/1.1/>
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX rdf:<http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX otee:<http://www.opentox.org/echaEndpoints.owl#>
PREFIX toxcast:<http://www.opentox.org/toxcast#>
```

```
select ?Feature ?title ?id ?assay ?geneid ?genename
where {
  ?Feature rdf:type ot:Feature.
```

```
{?Feature dc:title ?title}.
{?Feature owl:sameAs ?assay}.
{?assay toxcast:gene ?geneid}.
{?assay toxcast:hasProperty ?genename}.
{?genename rdf:type toxcast:GENE_NAME}.
}
```

Query an OpenTox ontology service at
<http://ambit.uni-plovdiv.bg:8082/ontology>

[http://ambit.uni-plovdiv.bg:8080/ambit2/dataset/961?feature_uris\[\]=http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335126](http://ambit.uni-plovdiv.bg:8080/ambit2/dataset/961?feature_uris[]=http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335126)



Feature	title	assay	geneid	genename
http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335126	ATO_RORE_CIS	http://www.opentox.org/toxcast#ATO_RORE_CIS	http://ibc2rdf.org/geneid/6095	http://www.opentox.org/toxcast#RORA
http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335187	ATO_LXRb_TRANS	http://www.opentox.org/toxcast#ATO_LXRb_TRANS	http://ibc2rdf.org/geneid/7376	http://www.opentox.org/toxcast#NR1H2
http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335132	ATO_MRE_CIS	http://www.opentox.org/toxcast#ATO_MRE_CIS	http://ibc2rdf.org/geneid/22823	http://www.opentox.org/toxcast#MTF2
http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335085	ATO_RARA_TRANS	http://www.opentox.org/toxcast#ATO_RARA_TRANS	http://ibc2rdf.org/geneid/5914	http://www.opentox.org/toxcast#RARA
http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335189	ATO_Eth_CIS	http://www.opentox.org/toxcast#ATO_Eth_CIS	http://ibc2rdf.org/geneid/2113	http://www.opentox.org/toxcast#NETS1
http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335090	ATO_NF_kB_CIS	http://www.opentox.org/toxcast#ATO_NF_kB_CIS	http://ibc2rdf.org/geneid/4790	http://www.opentox.org/toxcast#NFkB1
http://ambit.uni-plovdiv.bg:8080/ambit2/feature/335136	ATO_PBRM_CIS	http://www.opentox.org/toxcast#ATO_PBRM_CIS	http://ibc2rdf.org/geneid/9970	http://www.opentox.org/toxcast#BR13

Dataset and Ontology - find an assay, linked to specific gene

PREFIX ot:<<http://www.opentox.org/api/1.1#>>
 PREFIX ota:<<http://www.opentox.org/algorithms.owl#>>
 PREFIX owl:<<http://www.w3.org/2002/07/owl#>>
 PREFIX dc:<<http://purl.org/dc/elements/1.1/>>
 PREFIX rdfs:<<http://www.w3.org/2000/01/rdf-schema#>>
 PREFIX rdf:<<http://www.w3.org/1999/02/22-rdf-syntax-ns#>>
 PREFIX otee:<<http://www.opentox.org/echaEndpoints.owl#>>
 PREFIX toxcast:<<http://www.opentox.org/toxcast#>>

select ?Feature ?title ?id ?assay ?geneid ?gene

where {

?Feature rdf:type ot:Feature.

{?Feature dc:title ?title}.

{?Feature owl:sameAs ?assay}.

{?assay toxcast:gene ?geneid}.

{?assay toxcast:hasProperty ?genename}.

{?genename rdf:type toxcast:GENE_NAME}.

}



Query an OpenTox ontology service at
<http://ambit.uni-plovdiv.bg:8082/ontology>

Chemical compounds

Search results Dataset = 961 hits: 100

#	Compound	ToxCast At	Benigni /	Benigni /
		ATG RORE CIS	Structural Alert for genotoxic carcinogenicity	Structural Alert for nongenotoxic carcinogenicity
1		1000000.0	NO	NO
2		1000000.0	NO	NO
3		1000000.0	NO	NO
4		1000000.0	NO	NO

?feat

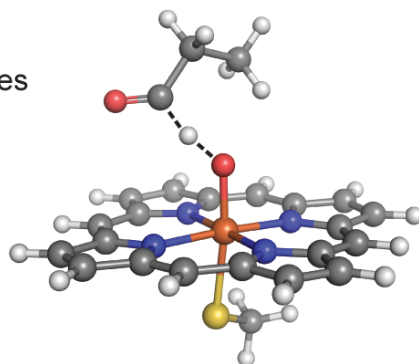
126

SMARTCyp Service for Predicting Metabolites

Atom Reactivity Library

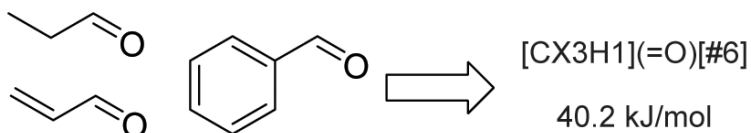
A. Calculate Quantum Chemical Reference Energies

Calculate transition state energies using density functional theory



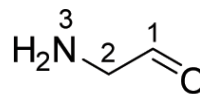
B. Define SMARTS Rules

Group calculations by fragments and calculate average energies



SMARTCyp

1. Assign Energies By SMARTS matching



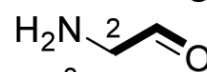
Atom	SMARTS	Energy
1	<chem>[CX3H1](=O)[#6]</chem>	40.2
2	<chem>[CX4][N]</chem>	39.8
3	<chem>[N^3][H1,H2]</chem>	54.1

2. Compute Accessibility Descriptor

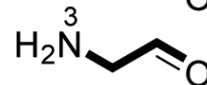
$$A_i = \text{Maxbonds}_i / \text{Maxbonds}_{\text{all}}$$



$$A_1 = 2 / 3 = 0.67$$



$$A_2 = 2 / 3 = 0.67$$



$$A_3 = 3 / 3 = 1.00$$

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

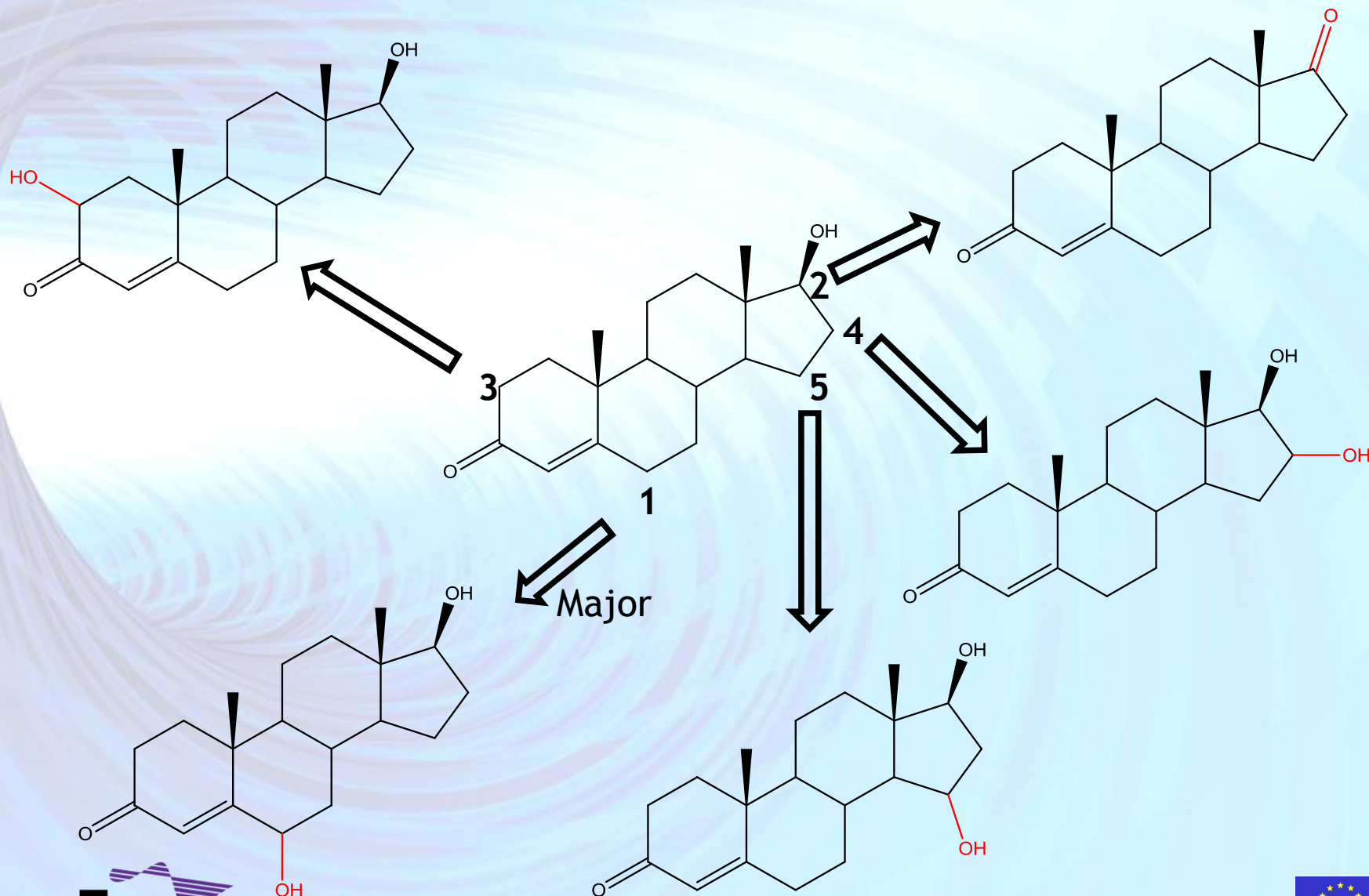
Atom 3 - Rank 3



SMARTCyp - developed by Patrik Rydberg, University of Copenhagen

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

SmartCYP Prediction of Testosterone Metabolites

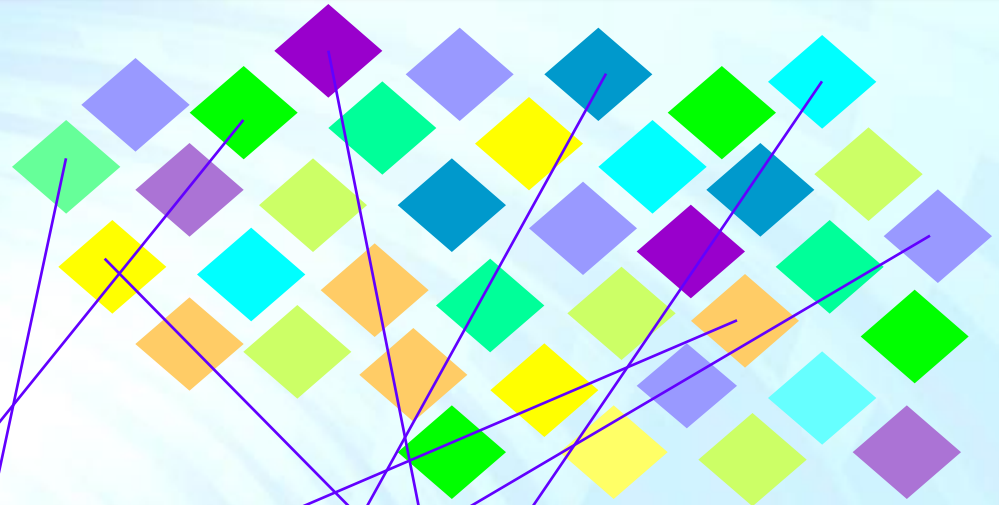


Creation of VO from Collaboration Pool

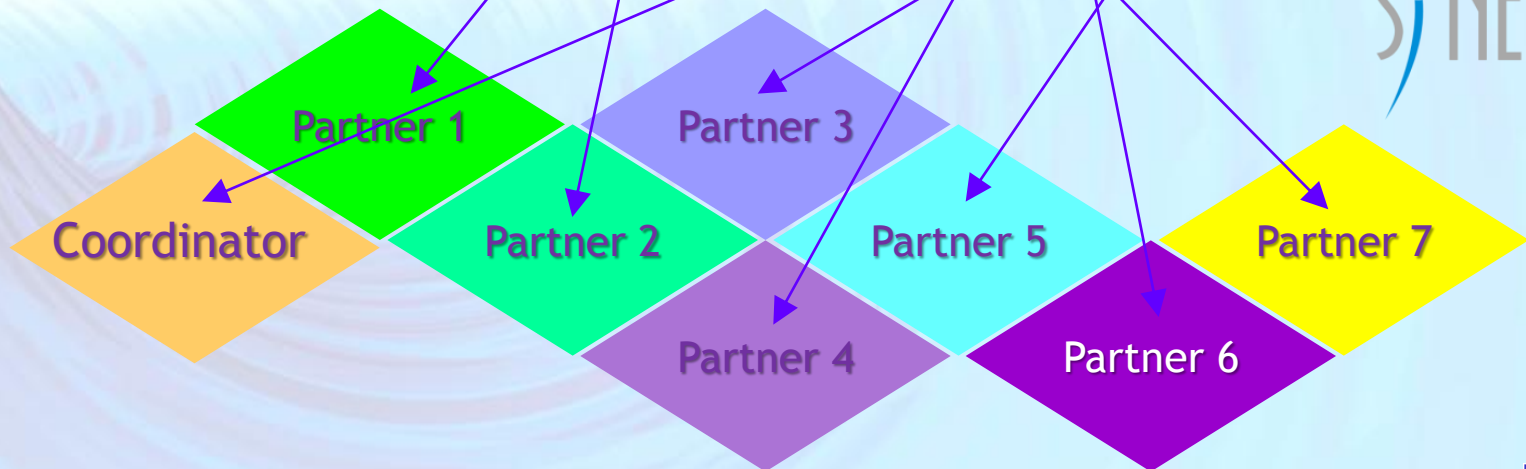
Network

Opportunity

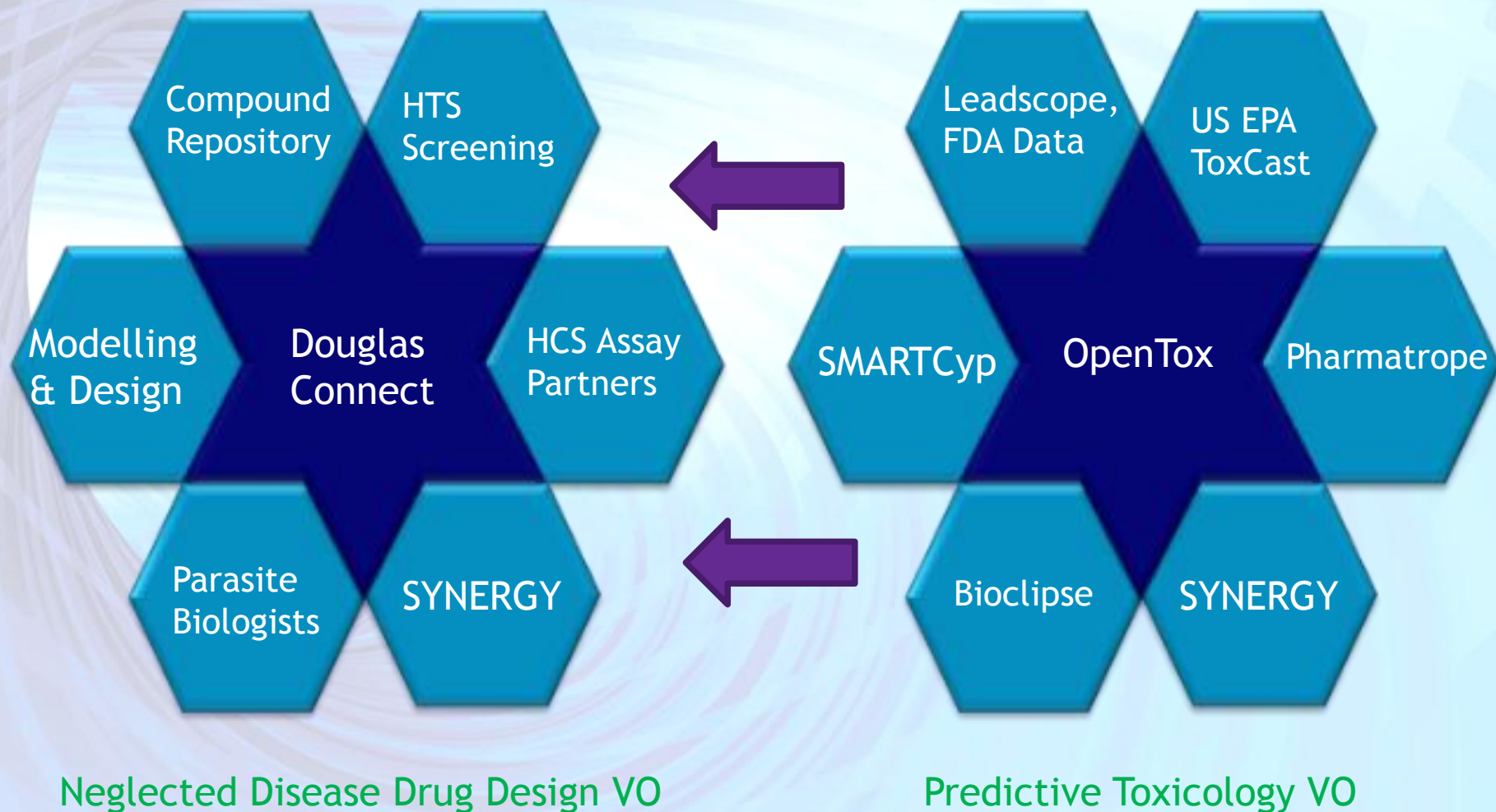
Call for Tender
Need for joint effort
Major project



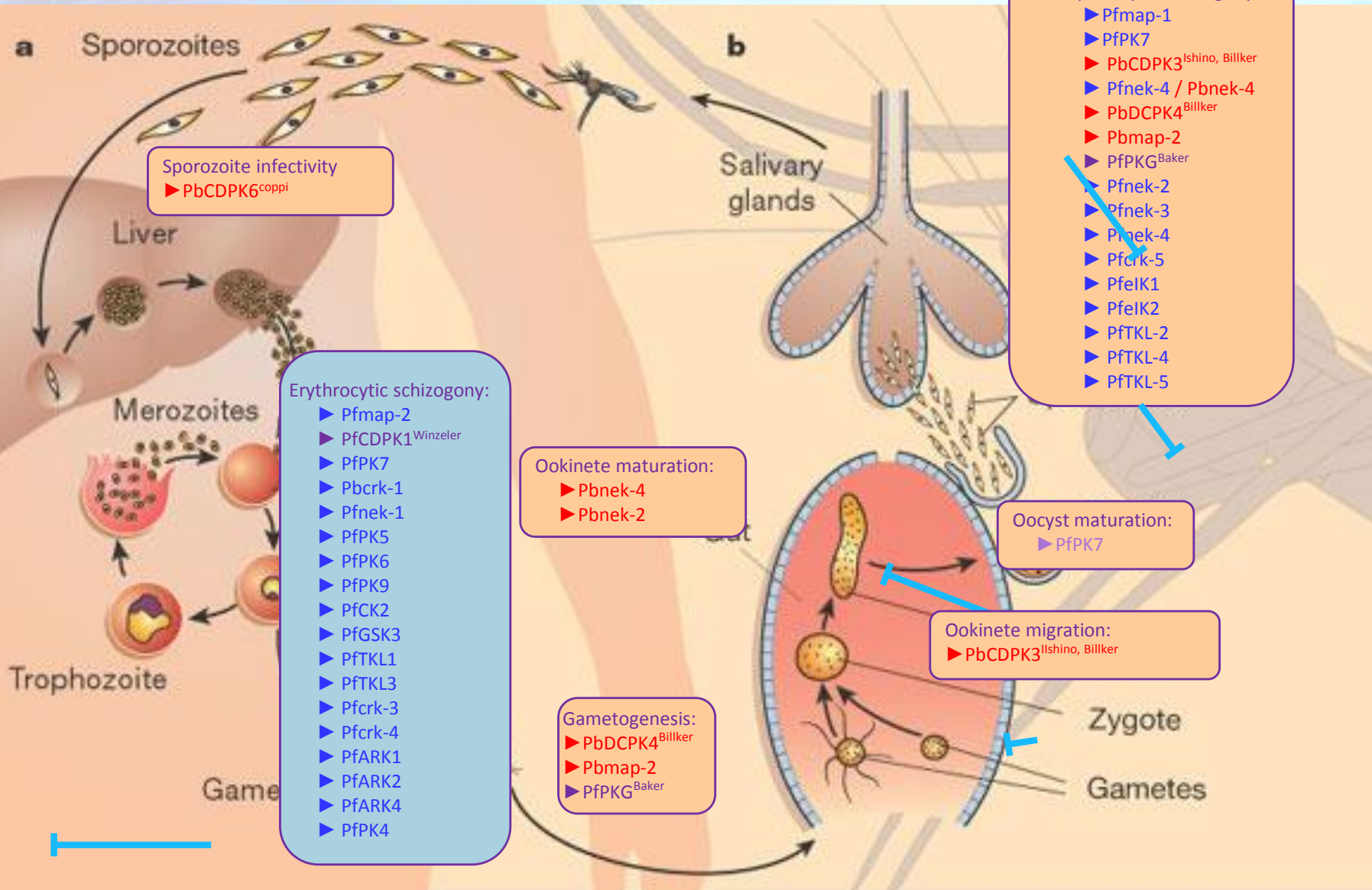
Virtual Organisation



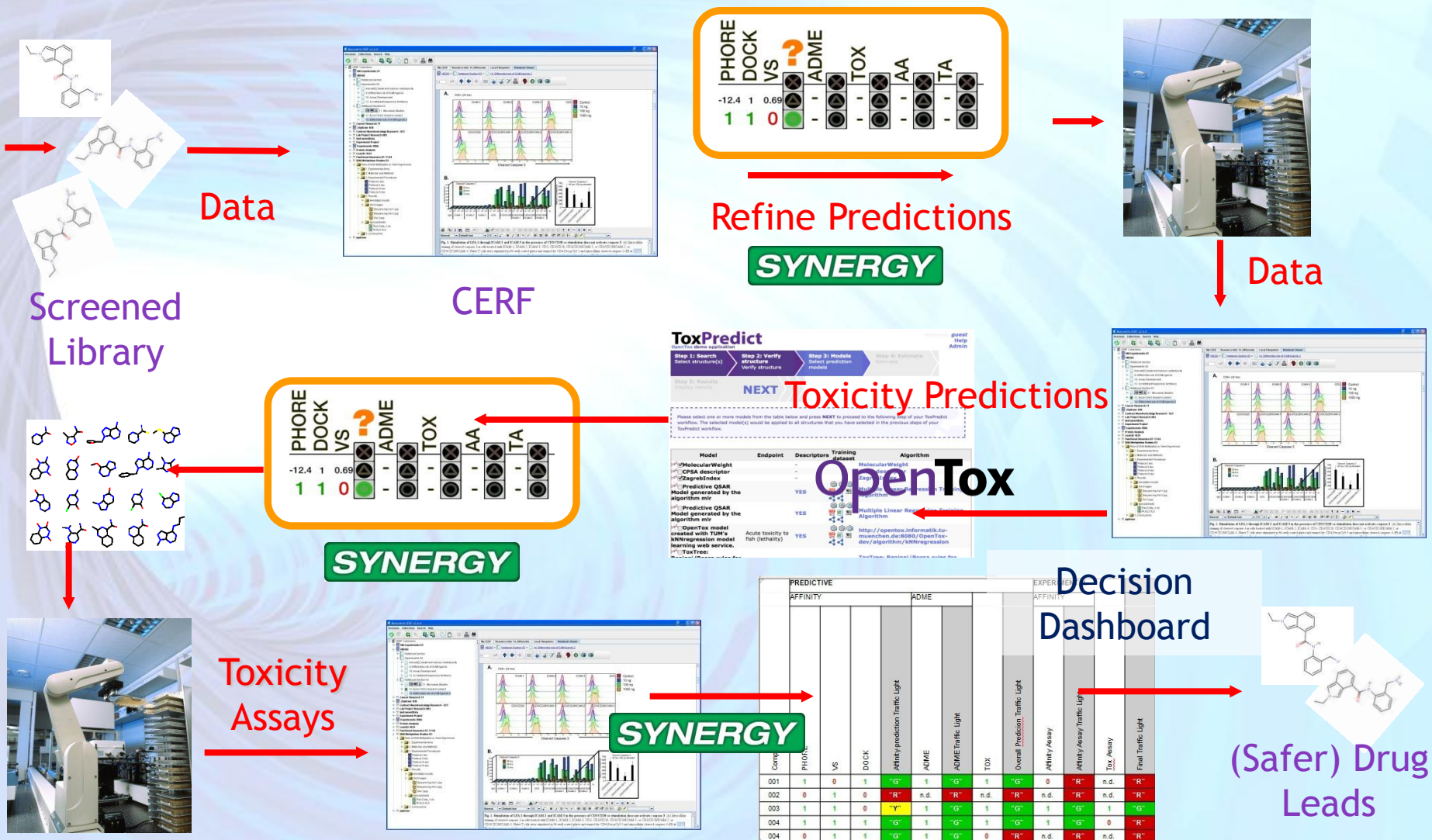
Virtual Organisation Pilots



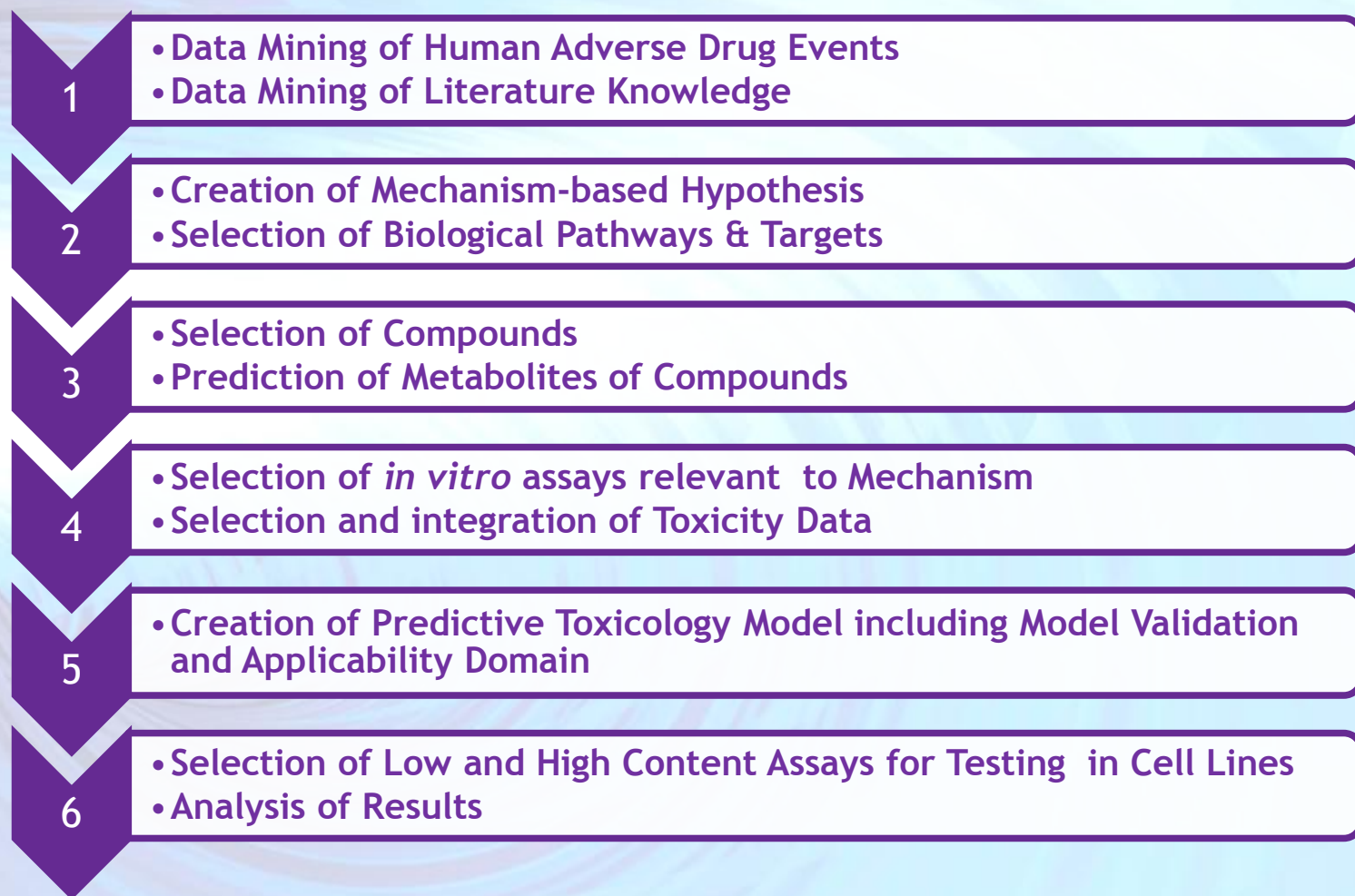
SAM VO targeting Plasmodium Kinases



Synergy Drug Design Collaboration Pilot

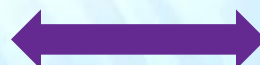
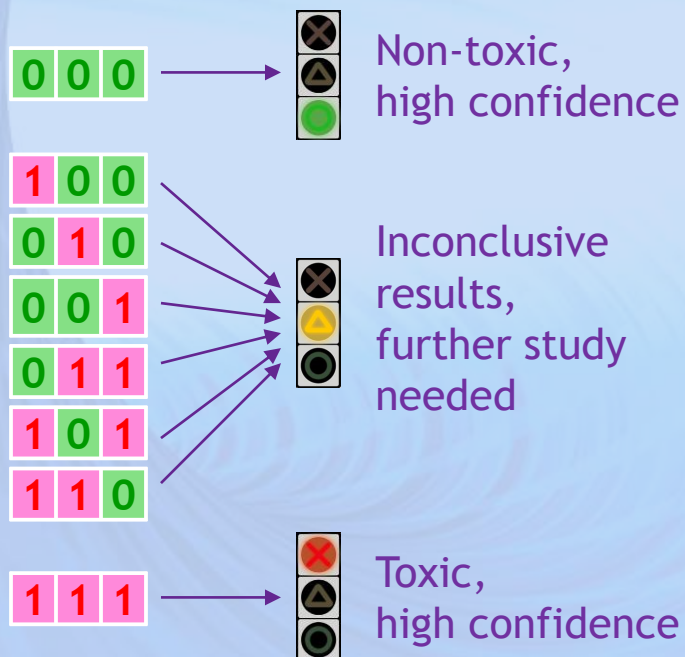


OpenTox - Synergy Predictive Toxicology VO Pilot Strategy Development & Case Study

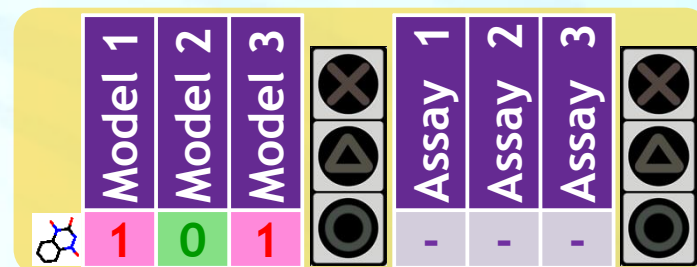


7. SYNERGY applies the Recommendation Rules

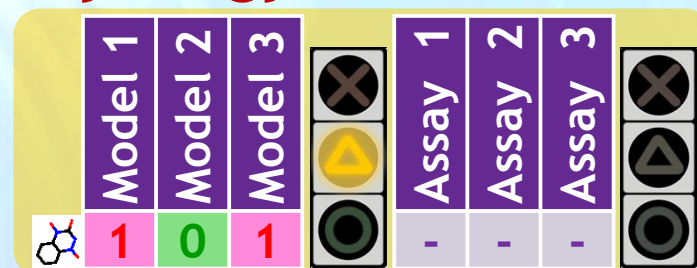
Recommendation Rules:



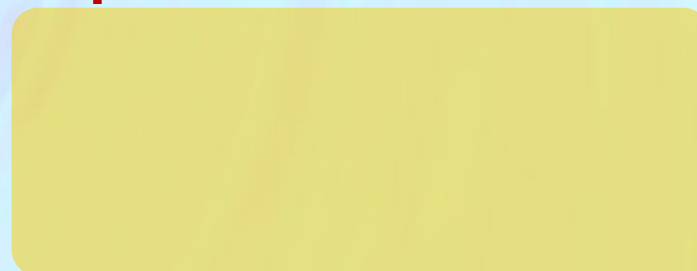
ELN



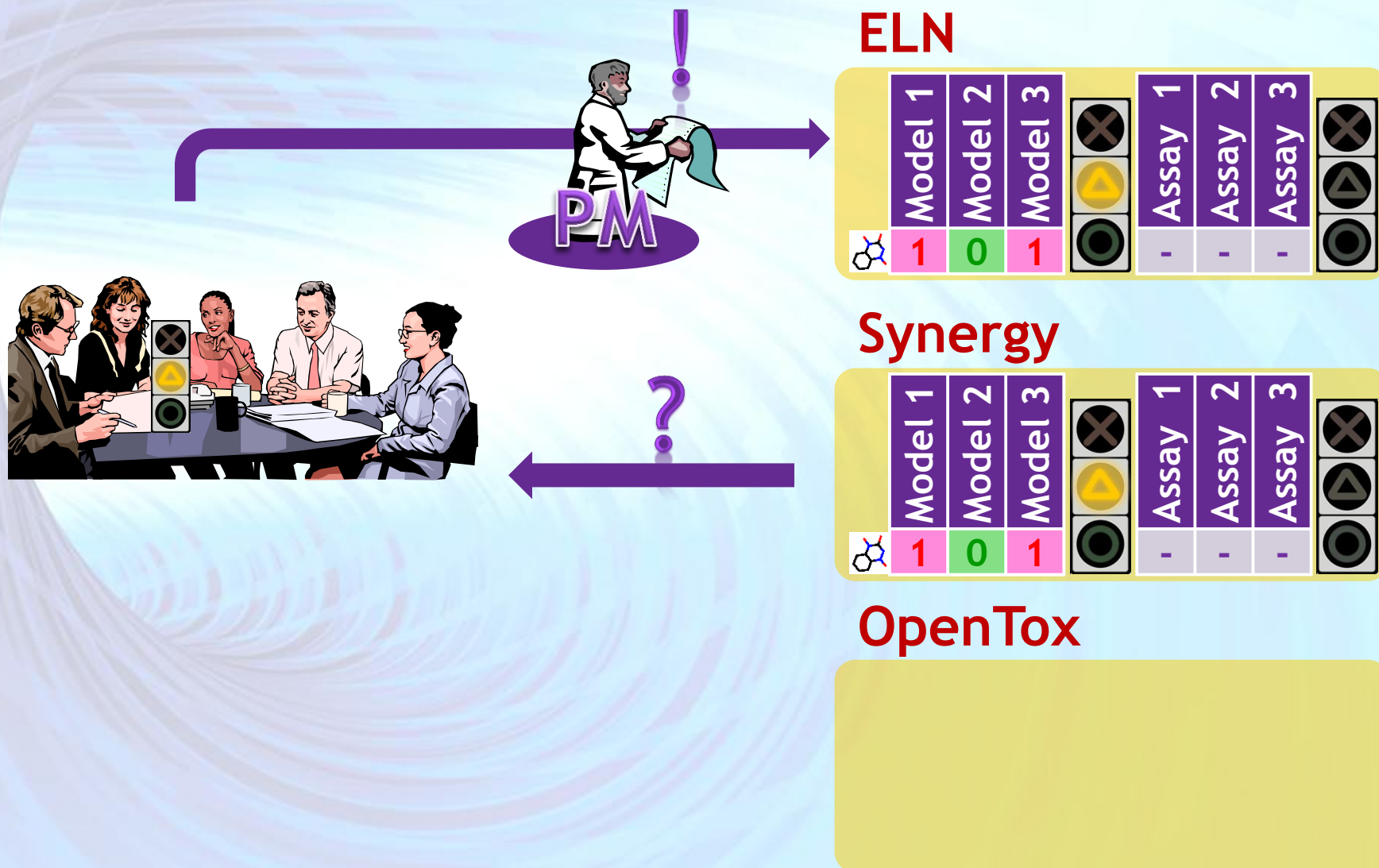
Synergy



OpenTox



8. Inconclusive data → SYNERGY calls a meeting



Pathways? - Taking on Technical, Cultural and “Other” Challenges of the Unexpected



[Visit with Lions at Mukuni Reintroduction Project, Livingstone, Zambia](#)

A Predictive Toxicology Pathways Question for us to discuss

How do we best leverage current knowledge and methods with regards to biological pathway analysis to design improved approaches to predictive toxicology that increase our ability to characterise the potential of chemicals to cause adverse human health effects and including an understanding of mode of action, mechanisms involved in the mode of action and the interaction of biological entities, pathways and networks in the perturbations introduced by the chemicals?

Time scales for developments

1. Short-term: 3 - 5 years
2. Medium term: 5 - 10 years
3. Long term: > 10 years

Discussion Elements relevant to developing directions for Pathways-based approaches

1. Contexts - Different contexts requiring different approaches...
2. Different Questions being asked by users (researcher, risk assessor, regulator...)
3. Strategies and Methods (Computational, in vitro, in vivo, combinations...)
4. Integrated Analysis - how to best carry out?
5. Infrastructure and Services - how to best support this interdisciplinary research and integrated analysis?

Contexts for Predictive Toxicology Methods

1. Pathway Known
2. Pathway Unknown and Rational Hypothesis is formed
3. Pathway Unknown and no Rational Hypothesis currently formed

Research areas from which methods could transfer and have potential impact

1. Which areas? - cancer research, systems biology, stem cell technology, pharmacokinetics,...
2. Which methods? What from Pathways methods?
3. Modifications and adaptations needs?

Lessons Learned in Pathways R&D

What have we learned from biological research related to pathways that could help avoid pitfalls and unpromising directions in pathways-based predictive toxicology approaches?

Choice of -Omics methods...

1. Genomics
2. Transcriptomics
3. Proteomics
4. Metabolomics
5. Cytomics
6. Epigenomics
7.

Which methods to select based on context? How do we best carry out an integrated analysis? What functional assays are needed?

Predictive Toxicology Variables to consider... (1)

1. Environment
2. Species
3. Sex
4. Age
5. Diet
6. Organ (s)
7. Drugs
8. Genetics
9. Healthcare record
10. In vitro vs in vivo ...

Predictive Toxicology Variables to consider... (2)

1. Organ, Organelle, Tissue, Cell - Cell Combinations
2. Metabolism
3. Cell (Type, differentiation)
4. Sub cellular compartments e.g., mitochondria
5. Concentration
6. Time
7. Dosage (amount, frequency)
8. Route of Administration
9. Reversibility of Toxicity effects
10. System interactions (local, non-local)

Final words...

For more information, visit

www.opentox.org

Contact me:

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**Many thanks for your
attention!**



OpenTox - An Open Source Predictive Toxicology Framework, www.opentox.org, is funded under the EU Seventh Framework Program: HEALTH-2007-1.3-3 Promotion, development, validation, acceptance and implementation of QSARs (Quantitative Structure-Activity Relationships) for toxicology, Project Reference Number Health-F5-2008-200787 (2008-2011).