



LRI ToolBox

EPAA ANNUAL CONFERENCE 2010

Dr. Bruno Hubesch

Cefic, Long-range Research Programme Manager



bhu@cefic.be
+32 2 676 7492



or...

14 Tools in a Box



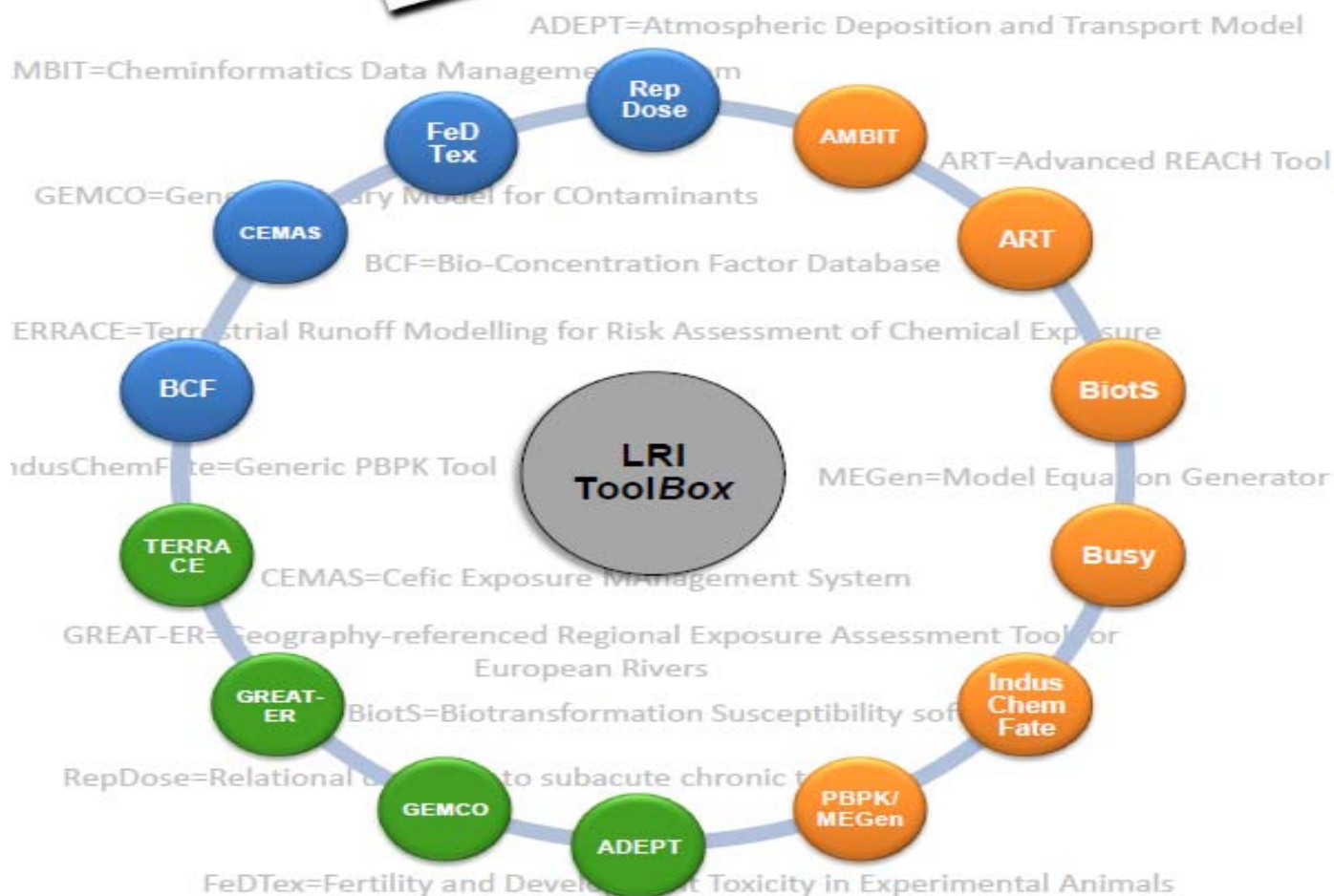
bhu@cefic.be
+32 2 676 7492



The LRI Toolbox



LRI ToolBox



LRI Toolbox



- Repository of 14 *alternative* tools (12y research)
 - State-of-the-art, easy to use, QA'ed
 - Freely available to all (web based, downloads)
- www.cefic-lri.org
- Organized by areas (human, eco, databases, models)
 - E.g. for RA and regulatory filing (REACH, GHS)
 - Significant animal use reduction +Mio Euro saving



LRI Toolbox

- Human health databases
- Human health models
- Environmental models



Human health databases

- CEMAS database
Cefic Exposure Management System
- FeDTeX
FErtility and Developmental Toxicity in Experimental Animals
- RepDose
Quality relational database for REPeated DOSE endpoints
(subacute to chronic toxicity)

RepDose



LRI
*The Long-range
Research initiative*

“Need a quality relational database for repeated dose endpoints ?”



Example: RepDose

Tuesday, 16 February 2010



The database for the analysis of relationship between chemical function groups/categories and target organs in repeated dose studies.

[User guide](#)

[About Repdose](#)

[Contact](#)

[Impressum](#)

Project partner



Please enter your email and password.

Email

Password

Project

Ambit



[Password forgotten](#)

[New member](#)



RepDose

- Relational database on subacute to chronic toxicity for repeated dose endpoints
- Developed Fraunhofer ITEM
- A relational database on exp. NOEL/LOEL values
- Contains QA'ed tox data on 655 chemicals (2300 studies)
- Useful in preparing dossiers and classifying compounds under REACH and GHS
- High usage (116 registered users only in 2010)
- www.fraunhofer-repdose.de



Human health models

- BiotS: Biotransformation Susceptibility software
- Busy: Bayesian Uncertainty SYstem
- IndusChemFate: Generic PBPK Tool
- PBPK/ MEGen: Physiologically-Based Pharmacokinetic Modelling / Model Equation Generator
- **AMBIT**
- **ART**

AMBIT



LRI
*The Long-range
Research initiative*

“ Need quality support for your decisions
by chemical grouping and QSAR? ”



AMBIT XT

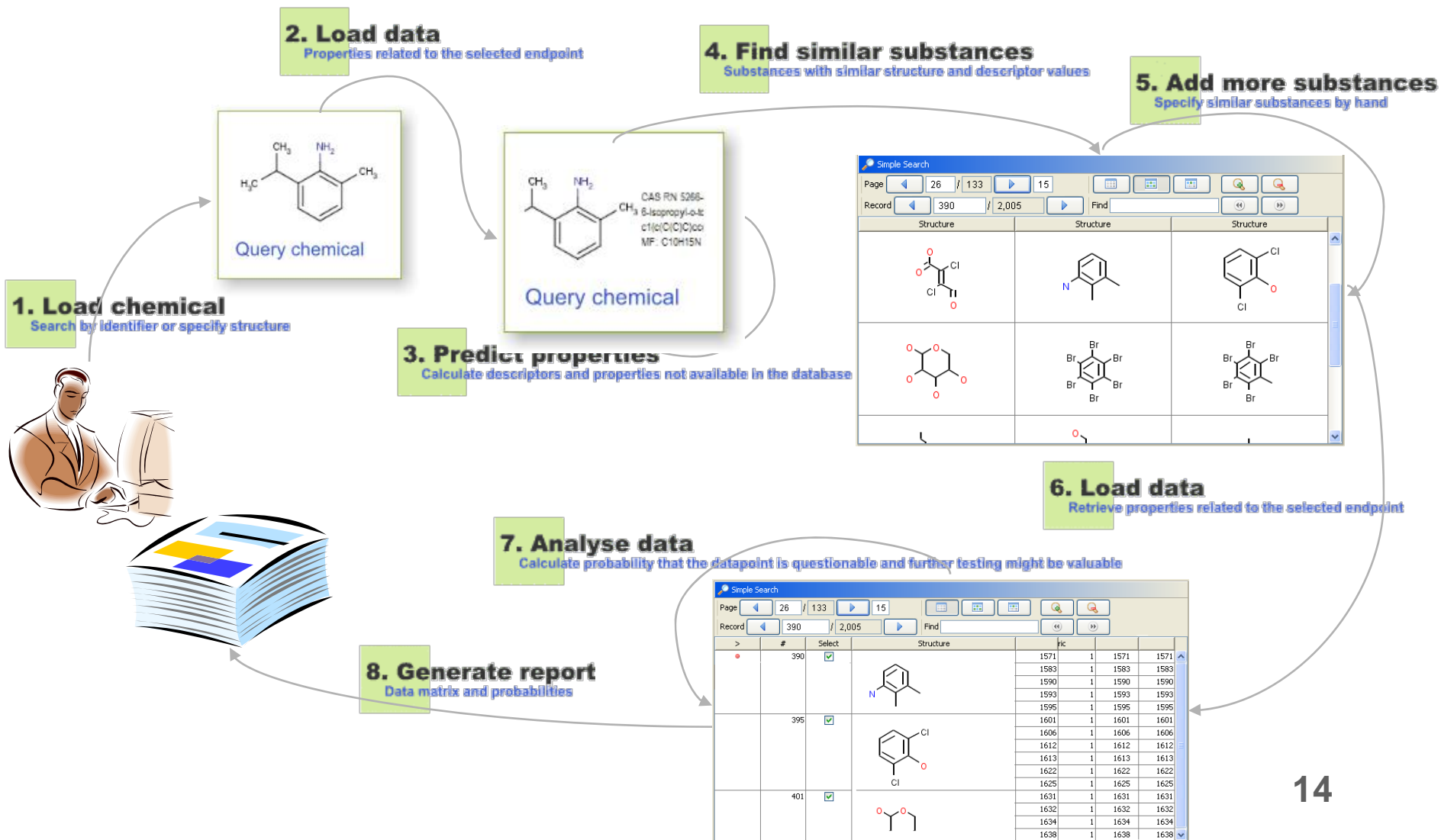
A computational tool for data management

AMBIT



- A software for chemoinformatic data management
- Developed by Cefic LRI, P&G, and IdeaConsult (BG)
- Stores more than 450.000 chemical structures and their identifiers such as CAS, Einecs, Inchi #'s
- REACH applicable PBT and analogues assessment
- Results preformatted REACH
- <http://ambit.sourceforge.net/>

Datapoint evaluation workflow



ART



LRI
*The Long-range
Research initiative*

“Need an inhalation exposure estimation model? ”

ART - Advanced REACH Tools



ADVANCED
REACH
TOOL

[My Scenarios](#)

[Science](#)

[Support](#)

[Consortium](#)

[English](#) | [Deutsche](#) | [Francais](#) | [Nederlands](#)

Welcome to the Advanced Reach Tool 1.0

Chemical Safety Assessments can be complex and time consuming. While Tier I models estimating exposure are available, should they be unable to show safe use, then refinement with more data or better assumptions is the only way forward. The Advanced REACH Tool (ART) version 1.0 incorporates a mechanistic model of inhalation exposure and a statistical facility to update the estimates with the user's own data. This combination of model estimates and data produces more refined estimates of exposure and reduced uncertainty.

The ART project has been conducted in close collaboration with a range of stakeholders from industry and member states. The use of ART for workers exposure assessment under REACH is described in ECHA' updated Guidance on [Information Requirements and chemical safety assessment](#).

ART can of course be used for exposure assessment in general, also beyond the REACH domain.

Contributors to ART



Existing users log in:

Email

Password

New user? [Register here](#).

Forgotten your password? Type in your email address above then [click here](#).

Latest News

History

First discussions on the need for a higher tier exposure model ... [\[more\]](#)

Future ART developments

ART is an evolving system that is anticipated to further develop in the future ... [\[more\]](#)

ART presentations

The basic concepts of ART and illustrative worked examples will be presented ... [\[more\]](#)

ART training

An ART training module is currently under development. It is anticipated ... [\[more\]](#)

ART



- Advanced REACH Tool
- Developed by TNO, HSL, IOM, BAuA, NRCWE and Utrecht University.
- A mechanistic and Bayesian model of inhalation exposure
- Facilitates higher tier exposure assessment under REACH guidance
- Simple, easy-to-use, cost-effective
- An ART training module is available
- <http://www.advancedreachtool.com/>



Environmental models

- ADEPT: Atmospheric DEPosition and Transport model
- GEMCO: Generic Estuary Model for Contaminants
- TERRACE: Terrestrial Runoff Modelling for Risk Assessment of Chemical Exposure
- GREAT-ER

Example: GREAT-ER

GREAT-ER web directly from here. Webapplication hosted by **Intevation GmbH**'."/>

GREAT-ER
GEOGRAPHY - REFERENCED REGIONAL EXPOSURE ASSESSMENT TOOL FOR EUROPEAN RIVERS

A GIS Assisted Model For Environmental Risk Assessment and Management of Chemicals in River Basins.

Publically available scientific software. Subject to the included End User Licence Agreement.

Start [GREAT-ER web](#) directly from here.
Webapplication hosted by **Intevation GmbH**

***GREAT-ER 1.0 (1999)** was sponsored by the Environmental Risk Assessment Steering Committee (ERASM) of the Association Internationale de la Savonnerie, de la Détergence et des produits d'Entretien (AISE) and the Comité Européen des Agents de Surface et de leurs Intermédiaires Organiques (CESIO), in cooperation with the UK Environment Agency and*

GREAT-ER



- Geography-referenced Regional Exposure Assessment Tool for European Rivers
- Developed by INTEVATION (DE), Cranfield Univ.
- A model for environmental risk assessment and management of chemicals in river basins
- Designed for use at a post-screening level under REACH and the EU Water Framework Directive (WFD)
- More than 8.000 visits in 2010! >50k accumulated
- www.great-er.org



LRI Toolbox: What's next?

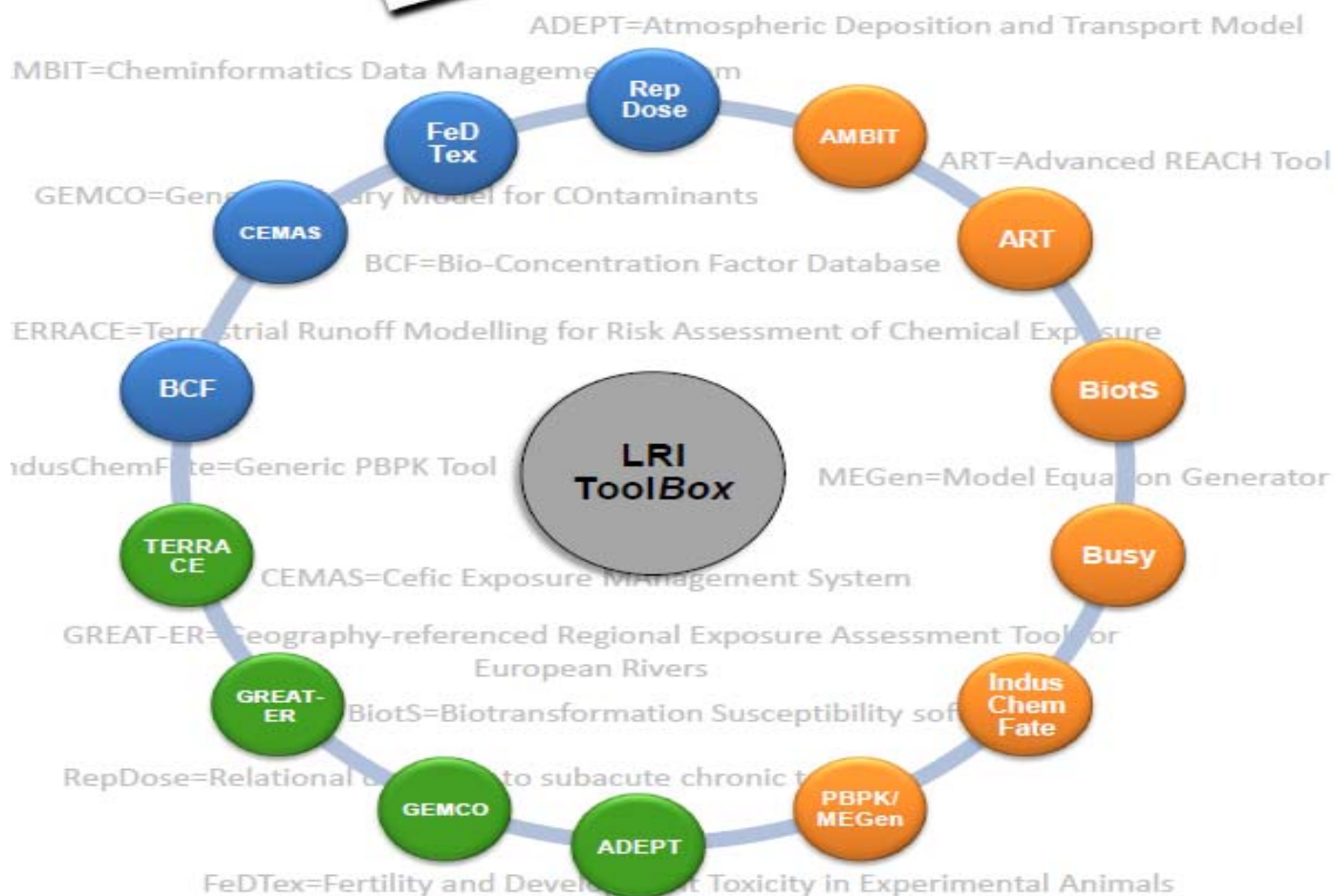
- Dissemination (ongoing)
- Transparency on key drivers for users
 - QA ?
 - Ease of use/Support ?
 - Applicability domain ?
 - Regulatory acceptance ?



The LRI Toolbox



LRI ToolBox





Levels of key drivers

Tools	Quality assurance	Applicability domain	User-friendliness	Support by regulators
Human health databases				
BCF database	Yellow	Yellow	Green	Yellow
CEMAS database	Orange	Yellow	Orange	White
FedTex	Green	Orange	Orange	Orange
RepDose	Green	Yellow	Green	Orange
Human health models				
AMBIT	Green	Yellow	Green	Yellow
ART	Yellow	Yellow	Yellow	Green
BiotS	Orange	Yellow	Orange	White
Busy	Yellow	Yellow	Orange	White
IndusChemFate	Yellow	Green	Yellow	Orange
PBPK/MEGen	White	Yellow	Yellow	Orange
Environmental Models				
ADEPT	Yellow	Orange	Green	White
GEMCO	White	White	White	White
GREAT-ER	Green	Yellow	Yellow	Yellow
TERRACE	White	White	White	White

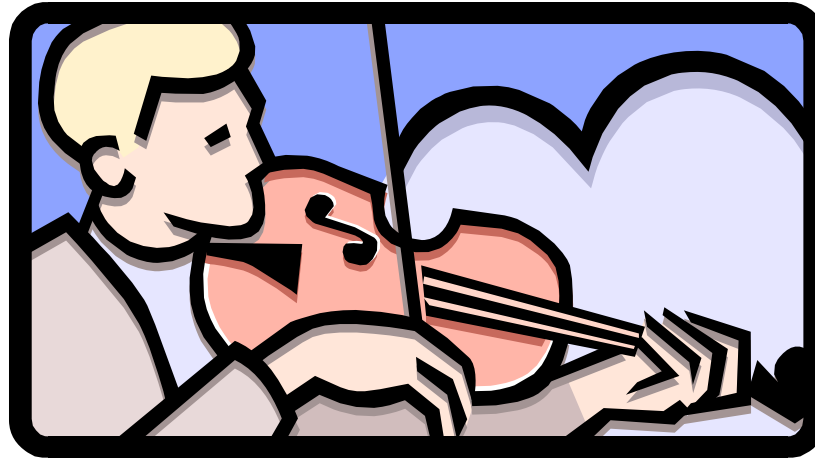
Green	very good/ very broad
Yellow	good/ broad
Orange	satisfactory/ limited/ pending
White	not applicable



What is next? *MegaBox?*

- Beyond LRI ToolBox: interlink + guidance on marketed alternative approaches
 - OECD Environmental RA Toolkit
 - OECD QSAR Application Toolbox
 - WHO Human Health RA Toolkit
 - OPENTOX
 - ECHA Information Toolkit (eChem Portal)
 - ECVAM *in-vitro* DB
 - FP QSAR modeling tools: ORCHESTRA (box)
(Ceasar, Osiris, Demetra, Scarlet, Rainbow,...)

THE END



Thank you !

Dr Bruno Hubesch
bhu@cefic.be
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Back-ups



AMBIT XT QA-ed datasets

- **EINECS list**
- **ECETOC Aquatic Toxicity (EAT) Database**
 - Supplement to ECETOC. 2003. Aquatic Hazard Assessment II. Technical Report No. 91. European Centre for Ecotoxicology and Toxicology of Chemicals, Brussels, Belgium
- **Bioconcentration factor (BCF) Gold Standard Database**
- **Compilation of historical local lymph node assay data for the evaluation of skin sensitization alternatives.**
 - Gerberick GF, Ryan CA, Kern PS, Schlatter H, Dearman RJ, Kimber I, Patlewicz G, Basketter DA. (2005). *Dermatitis* 16(4): 157-202.
- **Skin irritation and corrosion reference chemicals data base (1995)**
 - ECETOC Technical Report No. 66



Ambit - General overview

- **AMBIT software is a set of libraries and tools**
 - various chemoinformatics functionalities for data management
- **The AMBIT system consists of a database and functional modules**
 - providing multiple QA-ed datasets for REACH-relevant toxicological endpoints
 - allowing a variety of flexible searches and mining of the data stored in the database
- **The unique features of AMBIT**
 - ability to store multifaceted information about chemical structures
 - provide a searchable interface linking these diverse components.