

# Good Read-across Practices Workshop: Making it Work for You!

# **CEFIC LRI AMBIT Tool Supporting Read-across**

Dr. Volker Koch, Clariant CAAT EUTOXRISK LRI Workshop 26.02.2016

Public



# Introduction

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# Computational Toxicology (1)

#### >Non-testing approaches are used to fill gaps in Human and Environmental Safety Assessment (ECETOC, 2012 TR116) :

- ≻To avoid animal testing
- ≻Reduce resource costs
- ➢ Bridge the gap of laboratory capacity availability

#### Read-across and Category formation

- •Are Non-testing methods which are regularly applied to assess the safety of Chemicals and are accepted by most Regulatory Bodies if the approach taken is sufficiently justified and documented
- •Is supported by in-silico tools (see ECETOC, 2012, TR 116) using various methodologies like
- •QSARs, Expert systems allowing rule-based predictions, Similarity tools etc.



# Computational Toxicology (2)

- LRI AMBIT is an in-silico tool developed continuously since
   2005
- Goal of the LRI Project EEM9.3 was enhancing the predictive power of AMBIT
  - > Using large datasets of high quality Substance data
    - > From a IUCLID Database owned by a company itself
    - From ECHA IUCLID Database (non-CBI Disseminated data)
    - > From other reliable and quality checked data sources
  - Implementing workflows for Assessments supporting the assessor in setting up a read across/category approach and in establishing a valid justification for the approach taken as requested by authorities
  - Minimizing overall animal testing and resource costs means using available studies for other substances as well if appropriate

# Project overview



	ambit (************************************	
9     Exp (a)     Bit (b)     Bit (c)     Bit (c) <t< th=""><th>Data transfer View Search Assessments more induced by Admin Heip ( Welcome to AMBIT Ceffic Search address agents address in a work of the Search Admin Heip ( Welcome to AMBIT Centre of the search address in a work of t</th><th>AMBIT FUNCTIONS Assigning structures -to constituents, impurities Search structures &amp; Data</th></t<>	Data transfer View Search Assessments more induced by Admin Heip ( Welcome to AMBIT Ceffic Search address agents address in a work of the Search Admin Heip ( Welcome to AMBIT Centre of the search address in a work of t	AMBIT FUNCTIONS Assigning structures -to constituents, impurities Search structures & Data
Company IUCLID D ECHA IUCLID DB	B CEFIC LRI AMBIT Chemoinformatics	<ul> <li>exact, similar, substructure</li> <li>combined with data search</li> <li>Read across/category formation</li> <li>Workflows supporting the user</li> <li>Prediction tools</li> </ul>
As Major Data Source	e	-Cramer rules, Protein binding etc <b>Data analysis tools</b> -Regressions, clustering etc.
Search for data possible but not for structures	Supporting Read across & Category formation	<ul> <li>Data management         <ul> <li>flexible import/export of data</li> </ul> </li> <li>Data exchange         <ul> <li>manual or automated e.g.</li> <li>webservices</li> </ul> </li> </ul>



# IUCLID Data handling, Retrieval & Export

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# **IUCLID** Database

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#### **IUCLID Version 4** 3.5 Biodegradation -120. acrossed Inoculum: activated sludge, domestic, non-adapted Concentration: 200 mg/l related to Test substance Degradation: = 86 % after 28 day Result: readily biodegradable Kinetic: 15 dav > 10 % (1992)

	-	
	20 day = 60 %	
	25 day = 83 %	
Method:	other: gemäß OECD-Richtlinie	301 F (1
	(1994) und ISO 9408 (1991)	
Year:	1994	GLP: yes
Test substance:	other TS	
Source:	Hoechst AG Frankfurt/Main	
	Hoechst AG Frankfurt/Main	
	Clariant GmbH Frankfurt am M	lain
Test substance:	o-Anisidin; Reinheitsgrad: 99	9.4 %
Reliability:	<ol><li>valid without restriction</li></ol>	on
	Guideline Studie	

Manual Extraction of substance data to be used in read across/ category is rather straightforward

#### **IUCLID Version 5**

all fields 🔻	Results and di	scussions Overal	l remarks, attachn	nents Applicant'	s summary and con	clusion			
Administrati	ve Data				Ma	nual	Fxtr	actior	ר of
P						nuu		uotioi	
Purpos	e flag key study			9	sub	stand	ce d	ata to	be
Data wa	living					0.01			
data wa	iving				USE	d in ا	reac	lacro	122
Study result	t type experimen	tal result	۹ 🗸		uuu		l Cuc		001
Relia	ability 1 (reliable	without restrictio	n) 🔍 🔻		cated	iorv is	S CUI	mberg	some
Rationale for relia	bility Guideline s	tudy performed (	compliant to GLP.		outeg		5 00		001110
incl. deticie	ncies				ደ	time	con	eumir	חמ
Data source					C.	unic	CON	Summ	iy
Reference	1								
Reference type study report	Author Teufel &	Year 1994	Title Prüfung der	Bibliographic s unpublished	Hoechst AG,	93-0133-45	Clariant	93-0133-45	1994-03-02
	Voelskow		leichten biologischen Abbaubarkeit von o-Anisidin D	report of Clariant	Frankfurt-Höch st, Abt. Umweltschutz, D-65926 Frankfurt am Main				
Add	Edi	t	Delete	👚 Move up	Move down	n 🦉 Se	lect	insert 🖗	
Data access									
data submitter i	s data owner	4	•		4				
Data protection c	laimed	0			0	1			
yes, but willing t	io share				×				
≪ Degradatio	n of tast sub	₩ ₩	¥	Man	y pag	e scr	olls		
% Degi auatioi	%Degr.	stance	St.	dev.		Paramet	er		Sampling tir
86					O2 con	sumption		28 d	
10					O2 cons	sumption		15 d	
10									

IUCLID **4** had ca. **850** Database fields

#### s IUCLID **5** has **> 8500** Database fields



# **IUCLID Substance ID & Composition**

- > IUCLID Substance ID & Composition
  - > Every Substance in IUCLID is characterized by at least **one Composition**

**>**A IUCLID Substance composition has

**CONSTITUENTS** n>= 1, IMPURITIES n>=0, ADDITIVES n>=0

- >A <u>IUCLID substance</u> itself has <u>NO CHEMICAL STRUCTURE</u>. Only constituents, impurities and additives have a structure
- ➢As a IUCLID composition has at least 1 constituent, at least one structure is assigned. Very many IUCLID substances are related to more than 1 structure
- >When the IUCLID composition is transferred, AMBIT assigns automatically searchable structures to constituents, impurities and additives (if they are available in the AMBIT structure pool of > 400.000 structures)
- Most in-silico tools e.g. the OECD Toolbox cannot cope with the composition of a substances and relates <u>one</u> structure to a substance !



# IUCLID 5 Data retrieval & Transfer

### Endpoint data in IUCLID can be retrieved

≻"Manually"

➢ Using the IUCLID Query Tool

≻ Requires knowledge about the IUCLID data structure (experts only)

#### Structures in IUCLID are mostly

≻Images which cannot be retrieved and not be used for structures searches

#### > Manual Data Transfer

➤ Using the IUCLID 5 Bulk Export Assistant which is cumbersome requiring a multistep and manual interaction

### > Automated Transfer using Web services

≻IUCLID 5 and AMBIT are IT systems which are running on Web servers

>Web servers can interact via Web services allowing automated data transfer and update from IUCLD 5 not requiring manual interaction



# AMBIT Data import

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# Data Import filter for AMBIT

Substances > Import >	Retrieve substance(s) from IUCL	LID5 server	
Substance search ?	Retrieve substance(s) from IUCI	LID5 server	
Name	Select substance by UUID UUID*		
Search	Clear existing study records Import only high quality study reco Purpose flag 🍽 + -	Clear existing composition records ords Study result type <b>+</b> -	Test material 🏴 🕇 –
Study ? : <u>P-Chem</u> ENV ECO TOX	key study supporting study weight of evidence	experimental result experimental study planned estimated by calculation	yes no Not specified
Reliability ? : <u>1 2 3 4 5 6</u>	disregarded study Not specified	read-across based on grouping read-across from supporting sul 🔻	
Study purpose <b>?</b> : <u>K S</u> <u>WoE D N/A</u>	Reliability ■ + - 1 (reliable without restriction)	Reference type I■ + - study report	Select high quality study criteria
Robust study ? : Yes No	2 (reliable with restrictions) 3 (not reliable)	publication	+ <u>Select All</u> - Unselect all
Result ? : <u>E EP C RAg</u>	other:	secondary source	

> These filter allow to select which data from an IUCLID substance should be imported into AMBIT and work for manual or web based data import from IUCLID



# **AMBIT Chemoinformatics System**

Data & Structure handling Functions Communication

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- AMBIT Chemoinformatics System was developed within a CEFIC LRI Project in 2005 and is part of the LRI Toolbox
  - ➤Was continuously developed further and is now a state of the art Java web application running on all Operating Systems supporting Java
  - ≻Is an **Open Source Application** with the **following functions** 
    - Search for structure(s) [exact, similar, substructure] and meta data
    - Assessment tools (read across/category formation)
    - **Prediction tools** e.g. Cramer rules , Protein binding, pKa etc
    - **Data analysis tools** e.g. regression, classification, clustering etc
    - **Data exchange tools**: manual or automated via Opentox API, Webservices etc



### **AMBIT Search for Structures**

#### Exact, Similarity & Substructure



cefic

**Research Initiative** 





### Structures of Constituents, Impurities, Additives

- 4 -	64-17-5_Benzoic test substance 2 P4	acid_TRA0002_CLN _TST_DE00_REACH	IUC5-fae82ecc-	67 mono constitu substan	Benzoic acid ce		ECB5-172b9987-{	<u>S</u> <u>Claria</u> Prod (Deut <u>Gmb</u> Sulz! Taun <u>Gern</u>	antClariantukteGHS,tschland)ClariantH /GHS,bach amClariantus /GHS,nanyCompTox
	Comp Purity of IU	osition UUID: L-ab7 C Substance: 97-99	7c243-e03b-4cf1-8 % (v/v)	542-2a72ce3419	4a				
	Type 🔺	Name 🗍	EC No.	CAS No. 🔶	Typical concentration $\buildrel \oplus$	Concentrat	ion ranges 🛛 🔶		Structure 🔶
	Constituent	P Benzoic Acid,200-618-2	200-618-2	65-85-0	98 % (viv)	>97 % (wv)	<99 % (WV)	<u>Also</u> <u>contained</u> in	0 0
	Impurity	₽ Formaldehyde	200-001-8	50-00-0	1 % (WV)	>0.5 % (vv)	0.7 % (WV)	<u>Also</u> contained in	0



# **IUCLID Substance Data in AMBIT**

#### IUCLID Data in AMBIT are organized in tab sections allowing easy access by clicking on the tab of interest

IUC Substance Composition P-Chem	(6) Env Fate (1) Eco Tox (3) Tox (4)					
IUC Substance name:	Velsan SC_Sorbitane Caprylate_60177-36-8_TRA115477_ICS_MSe_Phase II_DE71					
IUC Substance UUID:	IUC5-e49aaecc-76d3-4f9f-b1b7-171fbff19363					
IUC Public name:	Sorbitane Caprylate					
Legal entity:	Clariant Produkte (Deutschland) GmbH / Sulzbach am Taunus / Germany					
Legal entity UUID:	IUC5-8da74af7-c7dd-4e38-8d8e-8fc765d5d15f					
Type substance composition:	UVCB					
IUC Substance Reference Identifier						
CAS:						
EC:	939-179-3					
Chemical name:	octanoic acid, esters with anhydrosorbitol and dianhydrosorbitol					
IUPAC name:	?					
UUID:	IUC5-a5f2fd8d-2e4b-413b-b785-2ec9104165d4					
IUC Flags:	Clariant EHS = TRA115477					
	CompTox = Ambit Transfer					



# **IUCLID Substance Data in AMBIT**

#### IUCLID Composition Data in AMBIT allow a straightforward overview on constituents, impurities & additives as well as the concentrations associated

IUC Substanc	e Composition	P-Chem (6)	Env Fate	(1) Eco Tox (3)	Tox (4)	-					
Compos Compo Purity of IUC	Composition name:Octanoic Acid, Esters With Anhydrosorbitol And DianhydrosorbitolComposition UUID:L-3b892463-4e89-4898-a5fc-b160cd3c46d8Purity of IUC Substance:45-100 % (w/w)										
Туре 🔺	Type Name EC No. CAS No. Typical Concentration ranges										
Constituent	P Octanoic Acid,124-07-2	204-677-5	124-07-2	0.8 % (w/w)	>=0 % (w/w)	<1 % (w/w)	Also contained in				
Constituent	<ul> <li>Unknown Organic</li> <li>Compounds, unknown</li> </ul>			ca.0.5 % (w/w)	>=0 % (w/w)	<1 % (w/w)	Also contained in				
Constituent	<ul> <li>Anhydrosorbitol,</li> <li>Triesters With</li> <li>Octanoic Acid</li> </ul>			4.2 % (w/w)	>0 % (w/w)	<10 % (w/w)	Also contained in				
Constituent	✤ Sorbitol, Mono- And Di-dehydrated			21.4 % (w/w)	>0 % (w/w)	<25 % (w/w)	Also contained in				
Constituent	<ul> <li>Sorbitol, Mono-</li> <li>And Di-dehydrated,</li> <li>Diesters With</li> <li>Octanoic Acid</li> </ul>			24.2 % (w/w)	>0 % (w/w)	<30 % (w/w)	<u>Also contained in</u>				
Constituent	<ul> <li>✤ Sorbitol, Mono- And Di-dehydrated,</li> <li>Monoesters With</li> <li>Octanoic Acid</li> </ul>			48.8 % (w/w)	>45 % (w/w)	<100 % (w/w)	Also contained in				

Showing 1 to 6 of 6 entries



# IUCLID Substance Data in AMBIT Data for 43 Endpoints from IUCLID

▼ P-C	hem	- Env	/ Fate	▼ Ecc	) Tox	🔻 Tox	
	🖬 4.1. Appearance ( <u>14</u> ) [18]		5.1.1. Phototransformation in Air (4) [4]	<b>V</b>	6.1.1. Short-term toxicity to fish (13) [32]	<b>V</b>	7.2.1. Acute toxicity - oral ( <u>15</u> ) [28]
	4.2. Melting point / freezing point ( <u>15</u> ) [20]	<b>V</b>	► 5.1.2. Hydrolysis ( <u>6</u> ) [6]	V	■ 6.1.2. Long-term toxicity to fish (4) [4]		7.2.2. Acute toxicity - inhalation ( <u>5</u> ) [8]
	➡ 4.20. pH ( <u>10</u> ) [11]	<b>V</b>	5.2.1. Biodegradation in water - screening tests ( <u>14</u> ) [32]	<b>V</b>	■ 6.1.3. Short-term toxicity to		7.2.3. Acute toxicity - dermal (6) [8]
	4.21. Dissociation constant ( <u>7</u> ) [10]		5.2.2. Biodegradation in water		aquatic inverterbrates ( <u>15</u> ) [24]		T.3.1. Skin irritation /
	🖀 4.3. Boiling point ( <u>15</u> ) [21]		(6) [6]		6.1.4. Long-term toxicity to aquatic inverterbrates (6) [8]		Corrosion ( <u>16</u> ) [30]
	4.5. Particle size distribution (Granulometry) (2) [2]		5.2.3. Biodegradation in Soil ( <u>5</u> ) [5]		6.1.5. Toxicity to aquatic algae and cyanobacteria (11) [18]		■ 7.4.1. Skin sensitisation ( <u>6</u> ) [9]
	🖀 4.6. Vapour pressure ( <u>12</u> ) [19]	<b>V</b>	5.3.1. Bioaccumulation: aquatic / sediment (5) [5]		■ 6.1.7. Toxicity to microarcapiems (10) [13]		7.5.1. Repeated dose toxicity - oral (7) [14]
	4.7. Partition coefficient ( <u>12</u> ) [21]		5.3.2. Bioaccumulation: terrestrial ( <u>4</u> ) [4]		■ 6.2. Sediment toxicity ( <u>5</u> ) [5]		7.5.2. Repeated dose toxicity - inhalation (5) [8]
	▲ 4.8. Water solubility ( <u>17</u> ) [23]		5.4.1. Adsorption / Desorption (5) [7]		6.3.1. Toxicity to soil macroorganisms (6) [7]		<ul> <li>7.5.3. Repeated dose toxicity -</li> </ul>
	solvents (10) [11]		5.4.2. Henry's Law constant ( <u>4</u> ) [4]		6.3.2. Toxicity to terrestrial arthropods ( <u>5</u> ) [5]	<b>V</b>	<ul> <li>7.6.1. Genetic toxicity in vitro</li> <li>(13) [33]</li> </ul>
					6.3.3. Toxicity to terrestrial plants ( <u>6</u> ) [6]		<ul> <li>7.6.2. Genetic toxicity in vivo</li> <li>(5) [11]</li> </ul>
					6.3.4. Toxicity to soil microorganisms (5) [5]		■ 7.7. Carcinogenicity ( <u>5</u> ) [5]

- 7.8.1. Toxicity to reproduction (<u>7</u>) [10]
- 7.8.2. Developmental toxicity / teratogenicity (8) [15]



IUC Substance	e Composition	P-Chem (6)	Env Fate (1)	Eco	Tox (3)	Tox (4)	_	_			
Filter								Expand all Collapse all			
Sorbitane Caj	prylate										
4.1 Appearance	(1)							•			
4.2 Melting poin	t / freezing point (1)							•			
4.3 Boiling point (1)											
4.6 Vapour pres	4.6 Vapour pressure (1)										
4.7 Partition coe	fficient (1)							•			
Value 🔺	Temperature	Å	рН	$\stackrel{\wedge}{=}$	Guid	leline 🔶	Owner 🔶	UUID 🔶			
= 2.55	= 23 ∘c		ca. 7		OECD Gui (Partition (n-octand Shake Fla	ideline 107 Coefficient ol / water), sk Method)	Clariant	IUC5-0068a11f-9274 ම			
Showing 1 study	r(s) (1 to 1)							◀ <u>Previous</u> <u>Next</u> ▶			
4.8 Water solub	lity (1)										
Value 🔺	Temperature 🔶	рН	Remark	\$	Guid	leline 🕴	Owner 🔶	UUID 🍦			
= 2.7 g/L	= 20 °C	[5.9, 6.4)	_		OECD Gui	ideline 105 Solubility)	Clariant	IUC5-818b7e62-efea 🄁			
Showing 1 study	(s) (1 to 1)										



### **IUCLID** Substance Data in AMBIT

IUC Subst	ance Co	mposition	P-Chem	(6) Env F	ate (1) Ed	co Tox (3)	Tox (4)	_	_		
Filter									Expand all Co	ollapse all	
Sorbitane	Caprylate										
5.2.1 Biodeg	pradation in v	vater - screer	ning tests (	1)						<b>^</b>	
Test type	Samplin time	<sup>g</sup> Degrada	tion Degr	ad. Paramete	r) result	<b>∲</b> Gu	ideline 🍦	Owner		•	
aerobic	= 28 d	= 88 9	% C	O2 evolution	readily biodegradab	OECD Gu (I le Biodegra Evolu	iideline 301 B Ready dability: CO2 tion Test)	Clariant Produ (Deutschland) Corporate Pro Stewardship on of BU ICS	ukte GmbH, duct behalf	0-1629	
Showing 1 s	tudy(s) (1 to	1)							Previous	Next 🕨	
IUC Subst	ance Co	mposition	P-Chem	(6) Env F	ate (1)	co Tox (3)	Tox (4)	)		_	
Filter									Expand all	Collapse al	
Sorbitane	Caprylate										
6.1.1 Short-1	term toxicity	to fish (1)									
Test 🔺 Medium	Organism	Meas. Conc.	Exposure	Endpoint	¢	Effect 🔶	Based on	Guideline 🍦	Owner	UUID	
		nominal	= 96 h	LC50	> 100 mg/L	mortality	test mat.	OECD Guideline	Clariant Produkte (Deutschland) GmbH		
freshwater	Danio rerio	nominal	= 96 h = 96 h	LC0 NOEC	= 100 mg/L = 100 mg/L	mortality mortality	test mat.	203 (Fish, Acute Toxicity Test)	Corporate Product Stewardship on beha	porate Product IUC5-21. ardship on behalf	
Showing 1 s	tudy(s) (1 to	1)							Previous	<u>Next</u>	



# IUCLID Substance Data in AMBIT

IUC Substa	ance Compo	sition P-Che	m (6)	Env Fate (1)	Eco 1	ox (3) Tox (4)		_	
Filter	- l.	]						Expand	all Collapse all
Sorbitane (	caprylate oxicity - oral (1)								
Species 🔺	Endpoint 🝦	Value 🔶	Sex	Interpretation of the results	criteria	Guideline 🔶	Study year	Owner 🍦	UUID 🔶
rat	LD50	> 2000 mg/kg bw	female	not classified	EU	OECD Guideline 423 (Acute Oral toxicity - Acute Toxic Class Method)	2009	Clariant	IUC5-aef4cde ලි
Showing 1 st 7.3.1 Skin irri	tudy(s) (1 to 1)	on (1)						◀ <u>Pr</u> e	evious Next
Meth	od type 🔺	Species	Interp	retation of the results	criteria	Guideline	Study year	Owner	UUID \$
in	vivo	rabbit	n	ot irritating	EU	OECD Guideline 404 (Acute Dermal Irritation / Corrosion)	2009	Clariant	IUC5-86bbb5 ®
Showing 1 st	tudy(s) (1 to 1)							Pre	evious <u>Next</u> 🕨
7.3.2 Eye irri	tation (1)								•
7.4.1 Skin se	nsitisation (1)								•



# **AMBIT Chemoinformatics System**

# Communication with other Systems

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# Workflow Read across & Category formation

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# AMBIT Workflows on Read across & Category formation





# Assessment Workflow in AMBIT Using a Tab Structure

	Assessment identifier	Collect structures	Endpoint data used	Assessment	details	Report
5 MAIN STEPS						
	Assessment identifier	Collect structures	Endpoint data used	Assessment d	etails	Report
7 SUB STEPS		Collect structure	s List of collected st	tructures		
_						
	Assessment identifier	Collect structures	Endpoint data used	Assessment details		Report
-			Search substance(s)	Selection of endpoints		
	Assessment identifier	Collect structures	Endpoint data used	Assessmer	nt details	Report
				Initial matrix	Working mat	rix Final matrix
_						
	Assessment identifier	Collect structures	Endpoint data used	Assessme	nt details	Report

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# New Assessment & Identifier

ambit 🕸 cefic Sea	rch • Assessments • In	nport 🔻	Enhanced function	s			
Home > All assessments >	New assessment	Use of Use of	empty template existing assessment	sessment details	Report		
1 1		itle 0:	Category justif	fication for Glymes			
	Ow	ner 🛛 :	user1				
	Purpo	ose0:	REACH Registration				
	Vers	ion 🛛 :	1				
	Version start da	ate 0:	03.08.2015				
	Version last modified	on 🔁 :	03.08.2015				
	Stat	tus 0:	Oraft versio	n 💿 Final assessmer	nt © Archived version		
	Assessment co	de 0:	\\sharepoint\R	EACH			
	Assessment Doclink	(s) 0:	VK-GLY01				
	Assessment	t ID 🔁 :	6b137267-39	b8-11e5-aa88-001e	e68a9cd90		
	Users with write acce	ess O:					
	Users with read acce	ess 0:					

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# Collect (Search) structures for Assessment

Assessment identifier Collect structures Endpoint data used Assessment details Report											
				Coll	lect structures List collected						
Search Exac	Search       Exact structure     Similarity     Substructure     URL										
Showing	Showing from 1 to 18 in pages of 20 entries  Previous Next Filter										
	Diagram	CasRN 🏺	EC number 🖗		Names		Rationale				
TS		97-90-5	202-617-2	ethylene dimethacrylate   2-Pro	penoic acid. 2-methyl 1.2-ethanediyl ester LE	thylene alycol					
CM				dimethacrylate							

T = Target, S = Source, CM = Category member

- Based on the Smiles code of the Target Diglyme a substructure search was carried out <u>limited to those having substance data</u>
- > Clicking T, S or CM allows to assign the structure for intended purpose

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### List collected structures for Assessment

Assessm	Assessment identifier Collect structures		ures Endpoir	Endpoint data used Assessment details Report						
				Collect structures List collected						
Showin	Showing from 1 to 3 in pages of 20 revious Next Filter									
T S CM		110-71-4	203-794-9	1,2-dimethoxyethane   Ethane, 1,2-dimethoxy-	Homologue of Target					
TS CM		111-96-6	203-924-4	diglyme   Ethane, 1,1'-oxybis 2-methoxy-   bis(2-methoxyethyl) ether   Ethane, 1,1'-oxybis[2-methoxy-   1-methoxy-2-(2-methoxyethoxy)ethane   1,1'-Oxybis[2-methoxyethane]   Diethylene glycol dimethyl ether   Ansul Ether 141   2,5,8-Trioxanonane   1,5-Dimethoxy-3-oxapentane   Diglyme   Dimethyl carbitol   2,2'-oxybis-, dimethyl ether   Dimethyl digol	Target					
T S CM		112-36-7	203-963-7	bis(2-ethoxyethyl) ether   diethylene_glycol_diethyl_ether   Ethane, 1,1'-oxybis[2-ethoxy-   1-ethoxy- 2-(2-ethoxyethoxy)ethane	Homologue of Target					

T = Target, S = Source, CM = Category member

Based on the Smiles code of the Target Diglyme a substructure search was carried out limited to those having substance data



### Search Substances associated to the Structures

Assessment	identifier	Collect structures Endpoint data	a used ous <u>Ne</u>	Assessment	details Report	ction (	of endpoints			Filter	Expand	all Collapse all	
	Diagram	CasRN		EC nu	ımber		Name	s		Rationale		Tag	
- 1 -	Showing from	110-71-4 1 to 3 in pages of 10 • substan	203- ces	203-794-9			1,2-dimethoxyethane   Ethane, 1,2-dimethoxy-			Homologue of Target		S	
	•	Substance Name	A V	Substance	Substance Type	\$	Public name	Reference substance UUI	D ≑	Owner	Info 🍦	Contained in as	
	▼ - 1 - ( ●	Slymes_Ethylene glycol dimethyl ether_(EGDME, Monoglyme)_ICS_MSe_[	DE71	<u>IUC5-eb8</u> €	mono constituent substan	nce	Monoglyme	<u>ECB5-73</u> ©	<u>Cl</u> Gn <u>Ge</u>	ariant Produkte (Deutschland) nbH / Sulzbach am Taunus / rmany		constituent	
	□ - 2 - 0 ■ 6	Slymes_Ethylene glycol dimethyl ether_(EGDME, Monoglyme)_ICS_MSe_[	DE71	<u>IUC5-eb8</u> … ੴ	mono constituent substan	nce	Monoglyme	<u>ECB5-73</u> ©	<u>Cl</u> Gn Ge	ariant Produkte (Deutschland) nbH / Sulzbach am Taunus / rmany		constituent	
	□ - 3 - () ■ e	Slymes_Ethylene glycol dimethyl ather_(EGDME, Monoglyme)_ICS_MSe_[	DE71	<u>IUC5-eb8</u> ੴ	mono constituent substan	nce	Monoglyme	<u>ECB5-73</u> ©	<u>Cl</u> <u>Gn</u> <u>Ge</u>	ariant Produkte (Deutschland) 1bH / Sulzbach am Taunus / rmany		constituent	

When clicking the Tab "Endpoint data used" associated substances can be display from the list and selected for further use (Subtab "Search substance(s)")



# Search Substances

Assessment identifier Collect structures	Endpoint data used Assessment details Report
Show all endpoints	Search substance(s) Selection of endpoints
▶ P-Chem	
▶ Env Fate	
▹ Eco Tox	
▼ Tox	
Showing 10 endpoint(s) (1 to 10)	
✓ 7.2.1. Acute toxic	ity - oral
7.2.2. Acute toxic	ity - inhalation
7.2.3. Acute toxic	ity - dermal
7.3.1. Skin irritati	on / Corrosion
7.3.2. Eye irritation	n
✓ 7.5.2. Repeated of	lose toxicity - inhalation
	kicity in vitro
	kicity in vivo
7.8.2. Developme	ental toxicity / teratogenicity
<b>7.999.9. Support</b>	ing information

When clicking the Tab "Endpoint data used" and subsequently Subtab "Selection of endpoints" a list of IUCLID Endpoints are displayed for selection by check marking 33 Public, CAAT EUTOXRISK LRI Workshop Dr. Volker Koch, Clariant, CEFIC LRI AMBIT Supporting Read across



# Working matrix (Composition section)

	CAS	Substance Name	ISUUID	Dete source	Teg	Diegrem	Constituent Name	Content	Contained As
• • •		Tetraglyme	<u>1005-541</u> B	Clariant Produkte (Deutachland)	5		112-49-2	2.4 % (w/w)	impurity 0
				Sulzbach am Taunus / Germany	T O	1	143-24-8	>55 % (w/w)	constituent O
				Ŧ	1		80.4 % (w/w)	constituent O	
•		Triglyme	<u>1005-203</u> B	Clariant Produkte (Doutschland)	8	ور م	112-49-2	co.90 % (w/w)	constituent 0
			Sulzbach am Taunus / Germany	5			>=99 % (w/w)	constituent O	
•		Monoglyme	anoglyme <u>IUCS-eb8</u> B	Clariant Produkte (Deutschland) GmbH /	5		1,2-dimethoxyethane	cc.97.8 % (w/w)	constituent O
				Sulzbach am Taunus / Gormany	5	5		>=99.9 % (w/w)	constituent O
					5	- La		cc.97 % (w/w)	constituent O
					5	هرير	111-96-6	cc.0.5 % (w/w)	impurity O
					5	<b>و</b> لرم م	112-49-2	cs.0.5 % (w/w)	impurity O
•		Diglyme	<u>1005-ი43</u> ზ	Clariant Produkte (Deutschland) GmbH / Sulzbach am	8	هرير	111-98-8	ca.92 % (w/w)	constituent 0
				Taunus / Germany	3	هر		>=99.9 % (u/u)	constituent 0

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# Working matrix (Endpoint section)

-	Assessment identifier Collect structures Endpoint data us					ised	Assessment details	s Report				
						L	Initial ma	trix Working matrix	Final matrix		Save	
	Identi	ifiers P-	CHEM ENV FATE	ЕСОТОХ	тох			_			Export	
	Showin	g from <b>1</b> to	<b>4</b> in pages of 20	<ul> <li>entries</li> </ul>	Previous Next	•				Filter		
		CasRN	Substance Name	I5UUID	Data source	Tag	Diagram ♦	n 6.1.1. Short-term toxicity to fish ♦		6.1.3. Short-term toxicity to aquatic inverter brates $$\frac{4}{7}$$	6.1.4. Long-term toxicit y to aquatic inverterbrat es	
	- 1 - T S CM		SiA_EC211-076-1_ 1,2-Diethoxyethan e_en	<u>IUC5-87c</u> ©	Example Company 1 / Example city / Finland	-	-	0		0	0	
	- 2 - T S CM •		bis(2-methoxyethy l)ether	<u>IUC5-fb67</u> ®	European Chemicals Agency / Helsinki / Finland	<b>T</b> 0	۾ آ	<b>0</b>		0	0	
	- 3 - T S CM		Diglyme	<u>IUC5-a43</u> ര	Clariant Produkte (Deutschland) GmbH / Sulzbach am Taunus / Germany	T O T O	۹ <b>(</b>	NOEC = 2000 mg/L  LCO > 2000 mg/L	(Exposure = 96.0 h) ❶ Exposure = 96.0 h) ❶	<ul> <li>EC0 &gt; 1000 mg/L</li></ul>	O <u>NOEC = 320</u> mg/L <b>⊄ û</b>	

3

4

5

5

2

Diglyme

Monoglyme



LD50 = 4760.0 mg/kg bw (rat)

LC0 = 11.0 mg/L air (rat)

# **EXCEL Export of Working Matrix**

EC10 =>= 1000.0 mg/L (growth rate ,Exposure=72.0 h)

NOEC =>= 1000.0 mg/L (growth rate ,Exposure=72.0 h) NOEC = 5000.0 mg/L (growth rate ,Exposure=72.0 h) ECS0 =>= 1000.0 mg/L (growth rate ,Exposure=72.0 h) EC10 =>= 1000.0 mg/L (biomass ,Exposure=72.0 h) NOEC =>= 1000.0 mg/L (growth rate ,Exposure=72.0 h)

EC50 =>= 1000.0 mg/L (biomass ,Exposure=72.0 h)

constituent

constituent

constituent

XI 📙	5 - ⊘ - ≩=	utu ≑				ma	trix.xlsx [Read-Only] -	Excel					O É É É É
FILE	CLARIANT HC	DME INSE	ERT PAGE LAYOUT	FORMULAS	DATA REVIEW VIEW	N							Volker Koch
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	Brandic		Clipboa	ard 🕞	Font	ra Align	nment	Fa Number f	Gells	Edit	ing		
B6	• E 🗙	√ fx	Monoglyme										
A	В	С	D	E		AB			AC			AI	AJ
1 Tag	Substance name	CAS No.	Structure	Contained as	6.1.5. Toxicity to aquatic a	algae and cyanobacteri	a 6.1.7	. Toxicity to microorganis	ms		7.2.1. Acute to	xicity - oral	7.2.2. Acute toxicity - inha
2				constituent									

EC10 => 1000.0 mg/L (Effect=respiration rate ,Exposure=3.0 h)

EC20 = 1067.0 mg/L (Effect=respiration rate ,Exposure=3.0 h)

6										
	AMBIT	has se	veral re	eporting for	unctions,	one is th	ne export	of the	Working r	natrix
	into EX	<b>KCEL</b> fo	r easie	r handling	g and prir	iting				

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### Assessment report



ambit 🕸 cefic	Search  Assessments  Import	Enhanced functions Admin Help							
$\underline{Home}\rangle\underline{Allassessments}\rangle\underline{Sim}$	This assessment $\langle$ Report $\rangle$								
Assessment identifier	Report								
Create Word file									
Ambit A	Ambit Assessment Report								
Category	ustilication for Ory	IIICS							
Author:	Unknown								
Company:	datamanageri 26.05.2015								
Assessment code:	64e268d4-12	22-4b5d-b121-71df4ba79df8							
Purpose:	REACH Regist	ration							
1. Assessn	ient Identifiers								
	Assessment title:	Category justification for Glymes							
	Owner:	Unknown							
	Purpose:	REACH Registration							
	Version:	1							
	Status:	draft							
	Version start date:	26.05.2015							
	Version last modified on:	26.05.2015							
	Published:	draft							
	Assessment code:	\\sharepoint\REACH							
	Assessment DocLink:	VK-GLY01							
	Assessment ID:	64e268d4-1252-4b5d-b121-71df4ba79df8							
The evidinal according to	in Analytican he found up "Accordent TD"								

The original assessment in Ambit can be found via "Assessment ID".

#### 2. List of structures for assessment

In the assessment, similar structures were selected from exact structure, substructure and/or similarity searches, or were added manually. The rationale for the selection is given in the table.

#### AMBIT has several reporting functions, one is creating an assessment report in Word



# **Project information**

Public

Dr. Volker Koch, Clariant CAAT EUTOXRISK LRI Workshop 26.02.2016

# **Project information**



> Project idea
 > LRI Manager
 > Contractors
 > Clariant Team for System design
 > Project finalized
 > Volker Koch, Ecotoxicologist Joachim Schneider-Reigl, Ecotoxicologist
 > December 8, 2015

#### DETAILED INFORMATION SEE LRI WEBSITE

LRI Workshop on AMBIT and READ-ACROSS 21 Jan 2016

<u>http://cefic-lri.org/events/lri-workshop-on-ambit-and-read-across/</u>



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CEFIC LRI would like to thank ECHA for providing the nonconfidential IUCLID data which are accessible on the ECHA Website



Datasets on <u>**14570</u>** Substances have been provided on January 12, 2016 by ECHA in Computer readable format allowing the import into AMBIT</u>