CADASTER

CAse studies on the Development and Application of in-Silico Techniques for Environmental hazard and Risk assessment

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Collaborative Project

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Overview of data on physicochemical properties, fate and environmental effects of chemicals within the four classes of chemicals selected
(Deliverable 2.1)

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Deliverable no: 2.1 (Overview of data on physico-chemical properties, fate and environmental effects of chemicals within the four classes of chemicals selected)
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Dissemination Level		
PU	Public	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	X

WP 2: Database on experimental parameters and (Q)SARs for chemical and biological endpoints

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Task 2.1- Overview of data on physico-chemical properties, fate and environmental effects of chemicals within the four classes of chemicals selected (Deliverable 2.1)

Overview

Existing experimental data for chemicals within the four classes of chemicals selected were collected on all endpoints of relevance for the environmental risk and hazard assessment. Physico-chemical properties, environmental fate parameters and aquatic and terrestrial ecological effects parameters, as well as different biological activities data are included on the most common regulatory endpoints considered in the Screening Initial Data Set Dossier (SIDS) and also other endpoints of relevance.

This task was carried out by means of literature searches, supplemented with searches of existing databases on risk and hazard assessment parameters. Additional data were requested from industry sources, amongst others via a request to the Research Institute for Fragrance Materials (RIFM) for substituted musks/fragrances and via a request to the Dupont Company for polybrominated diphenylethers (PBDE). Despite a number of efforts (email, telephone calls and telephone conferences, personal meetings) the response from industry was in general very limited and despite promises to provide data, not information at all was for instance received from RIFM.

The CADASTER project participants used the Online CHEmical database and Modeling (OCHEM) to introduce experimental data as well as the parameters that directly affect experimental findings. The database which was provided by Partner 6, HMGU, to the CADASTER project and allows the CADASTER users to submit, store, and annotate molecular records. The database thus allows for facile evaluation of the data within WP3.

The design of the database was completed in February 2009 (Deliverable 5.1). Thereupon, the database is filled with the relevant information on experimental data for chemicals belonging to the four classes of interest for the CADASTER project. The password-protected access to the CADASTER members is available at the project website www.CADASTER.eu.

Uploading the data in the database is a continuous activity which was performed for the chemicals currently in the database. This activity will be continued for all new chemicals that will be introduced in the database during the course of the project.

Activities performed

Existing experimental data on polybrominated diphenylethers (PBDE), perfluoroalkylated substances and their transformation products, substituted musks/fragrances, and triazoles/benzotriazoles were collected from the literature and from existing databases on physico-chemical properties, environmental fate parameters, and aquatic and terrestrial ecological effects parameters. The search was extended to additional biological activities of the chemicals of interest. Data on chemicals containing molecular structures which were considered relevant for the QSAR modelling (WP3) where also included in the database (for instance: data on flame retardants that are structurally different from the PBDEs that are the topic of interest within CADASTER, polyfluorocompounds in addition to perfluorochemicals, PFCs, etc.). The extension is essential to allow for application of read-across techniques in future stages of the project. All CADASTER project participants involved in data collection have already uploaded the corresponding experimental data in the Cadaster online database:

- Partner 1, RIVM, coordinated the data collection for substituted musks/fragrances
- Partner 2, PHI, coordinated the data collection for triazoles/benzotriazoles (TAZ/BTAZ)
- Partner 3, UI, collected and shared data for all four classes of chemicals
- Partner 4, IVL, coordinated the data collection for the polybrominated diphenylethers (PBDE)
- Partner 6, HMGU, collected and shared data from on-line databases for all four classes of compounds

The existing experimental data within the four classes of chemicals selected are thus available for use by the project participants.

There are two sets of molecules. The core datasets were provided by UI group. In these datasets all molecules were manually verified and annotated to the 4 CADASTER classes of molecules. There are in total 939 molecules in this set with 4994 records. These data will be the core data for model development.

The extended database was created by using simple fragmental definitions to extend the basic set. The selected molecules do not necessarily belong to our 4 classes, but could be used to extend the datasets with molecules having structural similarity. These data can be used to validate model for predictions outside of applicability domain as well as for read-across studies. This database includes the previous one and contains 7027 experimental data within the four classes of chemicals:

- Heterogeneous Brominated Compounds including 209 PBDEs and some other Flame Retardants: 721 structures and 2139 experimental data
- Perfluoroalkylated substances (PFC), including their transformation products: 1064 structures and 1617 experimental data
- Substituted musks/fragrances: 79 structures and 917 experimental data
- Triazoles and Benzotriazoles (TAZ/BTAZ): 461 structures and 2294 experimental data

All the details are available on the CADASTER website. The appendix to this report contains a summary of the data collected according to chemical class and according to group of endpoints. The appendix is arranged according to the four classes of chemicals identified within CADASTER.

One of the main conclusions that may be drawn from the detailed information given in the appendix (reflecting the data made available in the CADASTER database) is that in general the number of experimental data is quite large. However, in general only limited data are available for the endpoints of primary interest for environmental risk assessment within REACH, i.e. the SIDS endpoints. Especially data on adverse effects for relevant species are lacking and most toxicity are available for mammals (rats/mice). This again stresses the need for application of read across approaches on top of additional generation of data on SIDS endpoints already foreseen within the CADASTER project.

Activities foreseen

In line with the Description of Work of CADASTER, the set of experimental data that are collected and uploaded in the database will be expanded in the future. This can include extension of information on chemicals newly added to the database whenever this is required.

APPENDIX

The appendix to this report contains first of all a summary of the data collected according to the chemical class and the group of endpoints and is arranged according to the four classes of chemicals identified within CADASTER.

The database contains 7027 experimental data within the four classes of chemicals. All further details are available on the CADASTER website.

Brominated flame retardants, including BDEs (721 structures)

Endpoints - groups	*Number of data*
Physical Chemical Properties	1180
Environmental fate parameters	82
Aquatic and terrestrial ecological effects parameters	73
Other effect data	959
Total	**2139**

Perfluoroalkylated substances (PFC) (1064 structures)

Endpoints - groups	*Number of data*
Physical Chemical Properties	975
Environmental fate parameters	86
Aquatic and terrestrial ecological effects parameters	0
Other effect data	556
Total	**1617**

Substituted musks/fragrances (79 structures)

Endpoints - groups	*Number of data*
Physical Chemical Properties	259
Environmental fate parameters	104
Aquatic and terrestrial ecological effects parameters	108
Other effect data	446
Total	**917**

Triazoles and Benzotriazoles (TAZ/BTAZ) (461 structures)

Endpoints - groups	*Number of data*
Physical Chemical Properties	797
Environmental fate parameters	292
Aquatic and terrestrial ecological effects parameters	467
Other effect data	738
Total	**2294**

To illustrate the variance across the data collected for the various groups of endpoints, a more detailed division of data collected is made for the brominated flame retardants and the perfluoroalkylated substances:

1 - Brominated flame retardants, including BDEs

Physical Chemical Properties and Fate

Endpoint	*Units*	*Experimental data*
Boiling Point	[°C]	300-425
Melting Point (TM)	[°C]	48.5-206
S Water Solubility	[mol/L, 25°C] [mg/L]	0.0005-0.13
Vp Vapor Pressure	[Pa, 25°C] [mm Hg]	$1.7*10^{-7}$-0.0021
P_L Subcooled Liquid Vapour Pressure	[Pa, 25°C] [mm Hg]	$9*10^{-7}$-0.163
pKa Dissociation Constant		N/A
Atmospheric OH Rate Constant	[cm3/molecule-sec]	N/A
H Henry's Law Constant	[Pa m3/mol, 25°C] [atm-m3/mole]	0.04-4.8
K_{OA} Octanol-Air Partition Coefficient		7.34- 11.96
K_{OW} Octanol-Water Partition Coefficient		5.03-9.9
Koc Organic carbon-Water Partition Coefficient	[L/kg]	77 625- 630 9573
Ksed Sediment-Water Partition Coefficient		N/A

Data on toxicity and Ecotoxicity endpoints

Endpoint	*Units*	*Experimental data*
Subchronic mammalian toxicity (rat, mice), 28-106 days NOAELs, 9 entries on brominated flame retardants but only 1 for BDE congen	Feeding studies, mg/ kg bw, day	200-1 250
Aerobic degradation rates in soil. 6 entries on brominated flame retardants but only 2 for BDE-congeners	t½ days	10-360
Aerobic degradation rates in activated sludge. 9 entries on brominated flame retardants but only 1 for BDE congen,	%/ 28 days	0-1.4
Bioconcentration factors (Flow-through BCF) mostly on Cyprinus carpio or Pimphales promelas. 7 entries on brominated flame retardants but none for BDE-congeners	Dimensionless (Conc. in fish tissue/ Conc. in aqueous phase)	0.3-3000
Bioconcentration factors (Static, on blue mussels (*Mytilus edulis*). 2 entries on BDE congeners	mg dw/l	$1.3\text{-}1.6*10^{6}$
Biota Soil Accumulation factors, 28 days test	Dimensionless	0.3-6

in earthworm. 6 entries on brominated flame retardants but only 3 for BDE-congeners		
Chronic/subchronic toxicity towards green algae (Skeletonema costatum), 72-96 hr duration. 6 entries on brominated flame retardants but none for BDE-congeners	mg/l	0.0025-1.5
Acute/subchronic toxicity towards crustaceans (Daphnia magna and Nitocra spinipes), 48–144 hrs duration, LC50s and NOECs. 24 entries on brominated flame retardants but only 1 on a BDE congen (BDE 28). Altogether 10 accute LC50s and 15 NOECs	mg/l	0.002-1.1
Acute toxicity towards fish (Bluegill sunfish, Rainbow trout and, Fathead minnow), 48-96 hrs duration, LC50. 8 entries on brominated flame retardants but none for BDE-congeners	mg/l	0.4-1531
Reproductive toxicity in rats, 90-120 days oral feeding studies, NOAELs or LOAELs. 4 entries on brominated flame retardants but only 2 for BDE-congeners (BDE 47)	mg/kg bw day	0.7-9367
Teratogenicity in rats, 20 days, gestation day 6-15 or day 0-20, by gavage, NOAELs (maternal). 4 entries on brominated flame retardants but none for BDE-congeners	mg/kg bw day	500-1000

2 - Perfluoroalkylated substances (PFC)

The data given here are restricted to the chemicals that fall directly in the structural domain of perfluoralkylated substances only: aromatic compounds and substances that bear no substantial degree of fluorination are for instance not considered in this analysis:

Physical Chemical Properties and Fate

Endpoint	*Units*	*Number of experimental data*
Boiling Point	[°C]	6
Melting Point (TM)	[°C]	31
S Water Solubility	[mol/L, 25°C] [mg/L]	18
Vp Vapor Pressure	[Pa, 25°C] [mm Hg]	32
P_L Subcooled Liquid Vapour Pressure	[Pa, 25°C] [mm Hg]	0
pKa Dissociation Constant		16
Atmospheric OH Rate Constant	[cm3/molecule-sec]	27
H Henry's Law Constant	[Pa m3/mol, 25°C] [atm-m3/mole]	15
K_{OA} Octanol-Air Partition Coefficient		0
K_{OW}		0

Octanol-Water Partition Coefficient		
Koc Organic carbon-Water Partition Coefficient	[L/kg]	0
Ksed Sediment-Water Partition Coefficient		0

Toxicity and Ecotoxicological Toxicity

Endpoint	*Units*	*Number of experimental data*
Algae EC_{50}	[mg/L; mM]	21
Daphnia magna EC_{50}/NOEC	[mg/L]	8
Freshwater snails (*Physa acuta*) LC_{50}	[mg/L]	2
Freshwater planarians (*Dugesia japonica*) LC_{50}	[mg/L]	2
Green neon shrimps (*Neocaridina denticulate*) LC_{50}	[mg/L]	2
Midge (Chironomus tentans) EC_{50}	[mg/L]	1
Vibrio fischeri EC_{50}	[μM]	5
Fish (Rainbow Trout) LC_{50}	[mg/L]	3
Fish (Tilapia) EC_{50}/LC_{50}	[mg/L]	4
Fish (Bluegill sunfish) LC_{50}	[mg/L]	1
Fish (fathead minnow) LC_{50}	[mg/L]	1
freshwater African clawed frog EC_{50}/LC_{50}	[mg/L]	1
Aquatic macrophytes EC_{50}/IC_{50}	[mg/L]	5
Plant EC_{50}/IC_{50}	[mg/L]	6
Rat inhalation LC_{50}	ppm	50
Mouse inhalation LC_{50}	mg/m^3	39
Guinea pig inhalation LC_{50}	ppm	3
Monkey inhalation LC_{50}	ppm	3
dog inhalation LC_{50}	ppm	3
Rabbit inhalation LC_{50}	ppm	1
Rat inhalation LCL0	ppm	13
Mouse inhalation LCL0	ppm	10
dog inhalation LCL0	ppm	2
Rabbit inhalation LCL0	ppm	2
Cat inhalationLCL0	ppm	1
Monkey inhalation LCL0	ppm	1
Mouse oral LD_{50}	mg/kg/once	11
Mouse intravenous LD_{50}	mg/kg/once	11
Mouse intraperitoneal LD_{50}	mg/kg/once	20
Mouse subcutaneous LD_{50}	mg/kg/once	20
Rat oral LD_{50}	mg/kg/once	48
Rat intravenous LD_{50}	mg/kg/once	3
Rat intraperitoneal LD_{50}	mg/kg/once	6
Rat subcutaneous LD_{50}	mg/kg/once	1
Rat skin LD_{50}	mg/kg/once	4
Rabbit oral LD_{50}	mg/kg/once	2
Rabbit skin LD_{50}	mg/kg/once	7
Guinea pig oral LD_{50}	mg/kg/once	1
Quail oral LD_{50}	mg/kg/once	1
Dog oral LD_{50}	mg/kg/once	1
Duck oral LD_{50}	mg/kg/once	2
Man oral LCL0	μL/kg/once	1
Mouse intraperitoneal LCL0	mg/kg/once	1
Rat oral LCL0	mg/kg/once	6
monkey oral LCL0	mg/kg/once	1
Dog intravenous LCL0	mg/kg/once	1

Dog oral LCL0	mg/kg/once	1
Rabbit oral LCL0	mg/kg/once	1
Fog Subcutaneous LCL0	mg/kg/once	2