Comprehensive screening of industrial chemicals to identify environmental contaminants

Michael McLachlan
11 October 2010

other project participants
Jon Arnot, Trevor Brown, Frank Wania (U. of Toronto)
Knut Breivik (U. Of Oslo)
Anna Malmvärn, Michael Radke (Stockholm University)

Stockholm University

The Problem

- In the past we have most commonly identified organic environmental contaminants by “chance”
- Can we find a more systematic way of identifying them?

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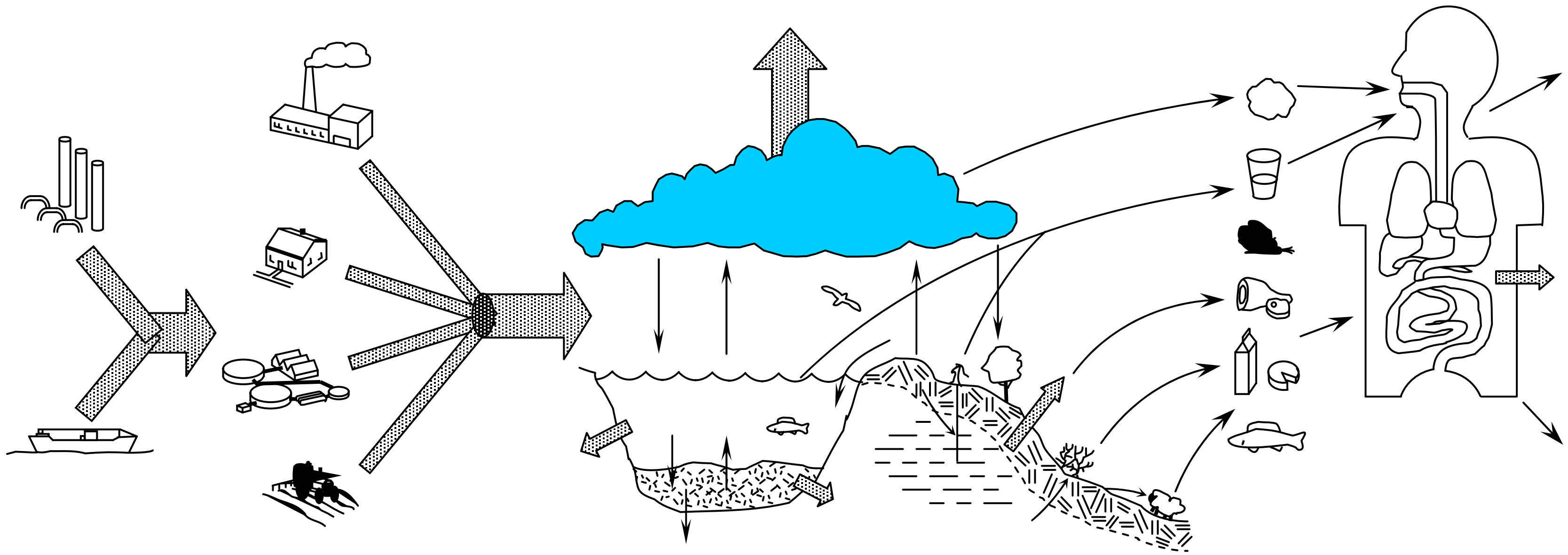
- Can we find a more systematic way of identifying them?
- >40 000 industrial chemicals in use
- Information on occurrence in the environment limited to a very few
- Cost of measuring new chemicals in the environment is high
- Can we find good methods of prioritizing chemicals for investigation?
- Focus on exposure

Human far-field exposure



Chemical emissions

Environmental fate/transport, distribution, degradation, food web bioaccumulation and exposure to humans

Mackay 2001

Linked environmental fate and exposure models

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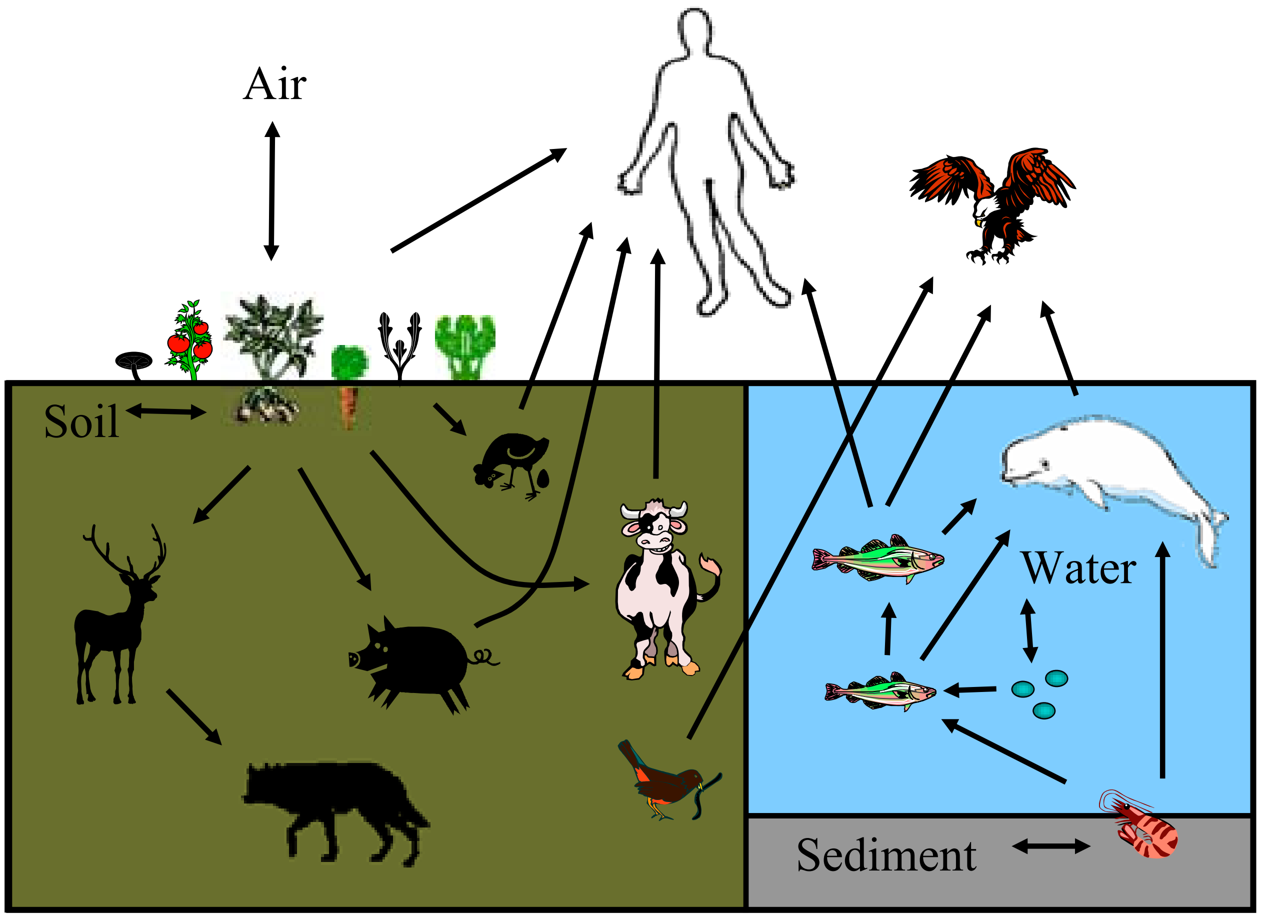
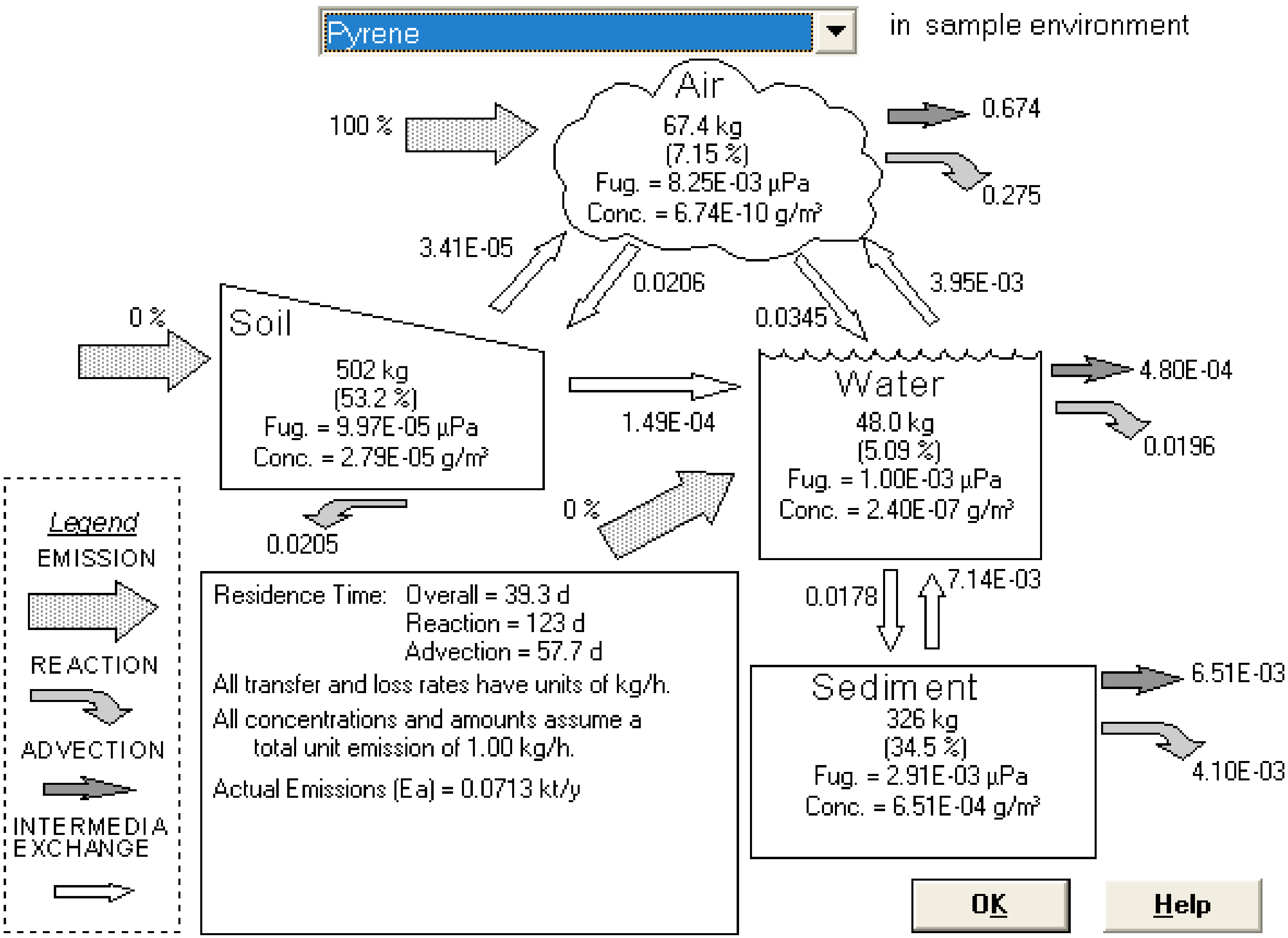


Environ Sci & Technol 40, 2316-2323 (V.1.0)

Environ Sci & Technol 42, 4648-4654 (V.2.0)

e.g., RAIDAR Level III fate model



Mechanistic bioaccumulation models

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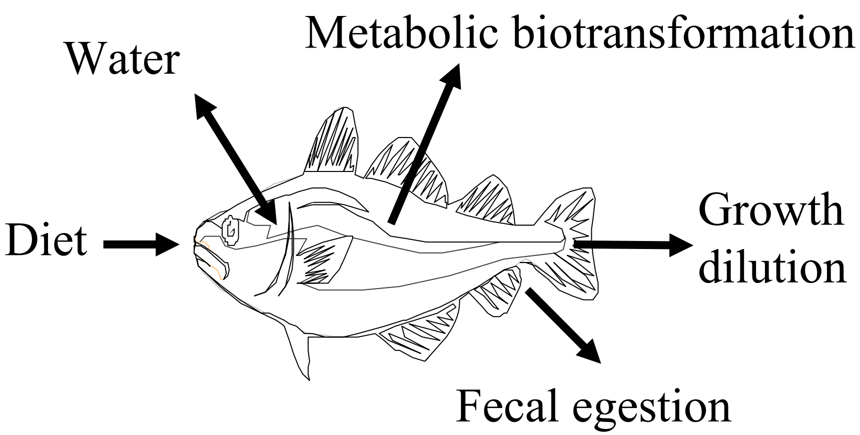
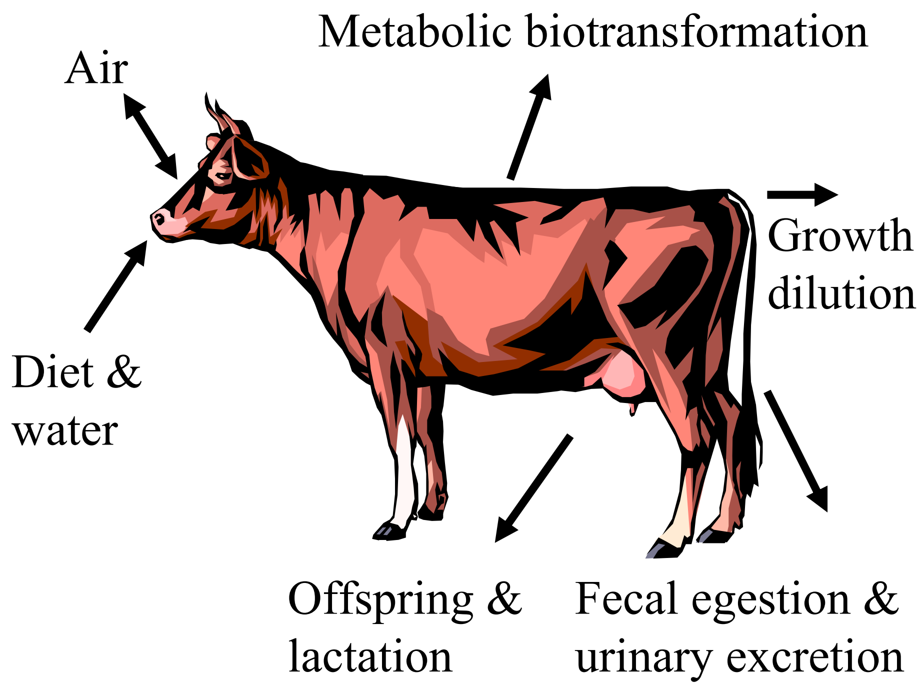
Bioaccumulation: competing rates of chemical uptake and elimination including bioconcentration and biomagnification

Water respiring organisms



Air breathing organisms



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Our endpoint:
Internal exposure in humans

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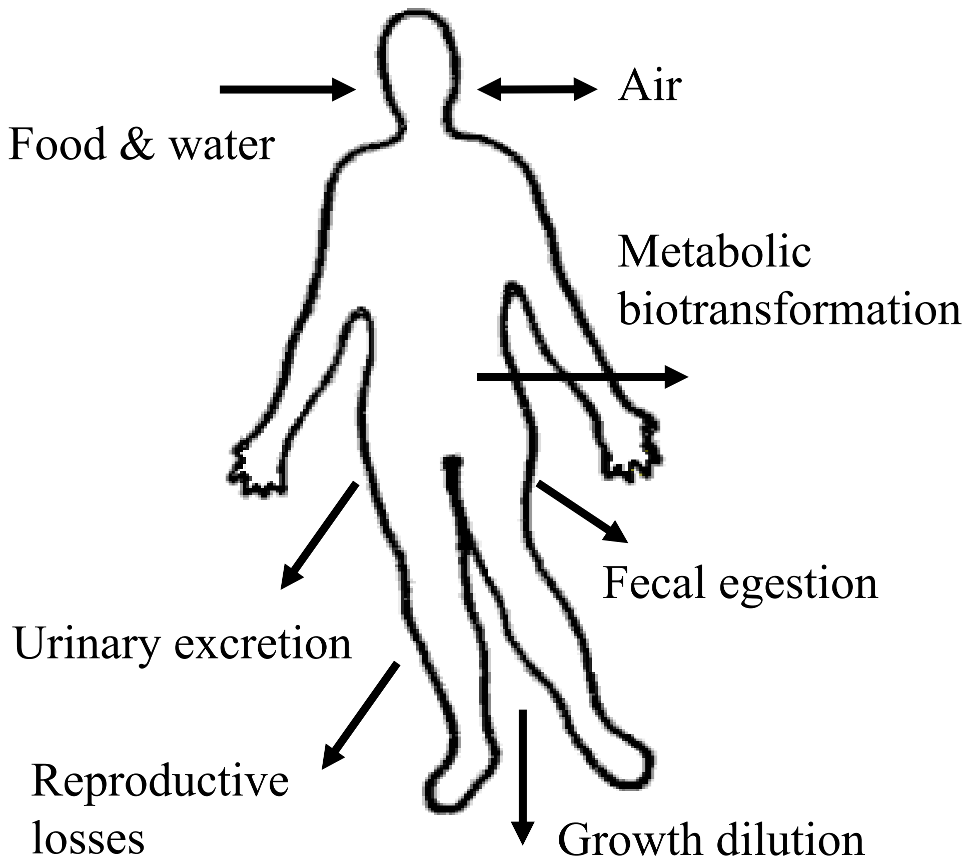

The list of chemicals to screen

ESIS	*N*	%
HPVC (> 1,000 t/yr)	2,781	26.2
LPVC (10 - 1,000 t/yr)	7,829	73.8
SUM (> 10 t/yr)	**10,610**	**100**

CDSL	*N*	%
HPVC (> 1,000 t/yr)	2,026	18.4
LPVC (1 - 1,000 t/yr)	9,013	91.6
SUM (> 1 t/yr)	**11,039**	**100**

Japan	*N*	%
1,000,000 – 10,000,000 t/yr	14	2.1
100,000 – 1,000,000 t/yr	47	7.1
10,000 – 100,000 t/yr	126	18.9
1,000 – 10,000 t/yr	478	71.9
SUM (> 1,000 t/yr)	**665**	**100**

US-EPA IUR 2006	*N* (2006)	%
> 453,592 t/yr	371	6.4
22,680-453,592 t/yr	175	3.0
4,536-22,680 t/yr	588	10.1
454-4,536 t/yr	1,372	23.6
227-454 t/yr	560	9.6
<227 t/yr	2,748	47.3
SUM (> 0 t/yr)	**5,814**	**100**

OECD	*N*	%
> 1,000 t/yr	**4,843**	**100**

All lists	*N*	%
	24,142	**100**

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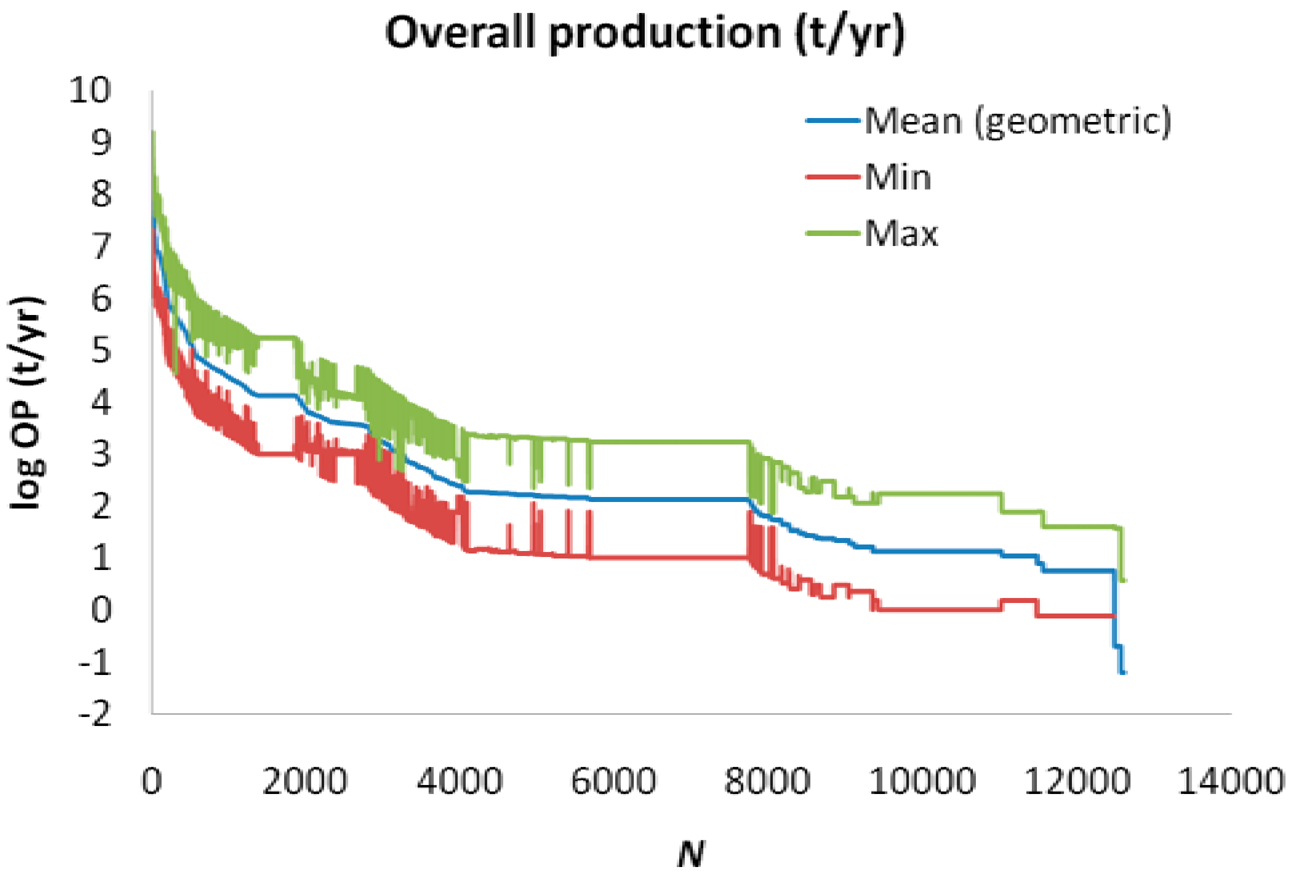
12,619 unique chemical structures for organics

Input requirements for C_H calculations

- Emissions
- Partitioning properties: K_{OW} & K_{AW}; $K_{OA} = K_{OW} / K_{AW}$
- Reaction half-lives (*HL*): air, water, soil, sediment
- Biotransformation half-lives in vertebrates

Estimating emissions: Tier 1



Estimating emissions: Tier 1

Default emission factor (TGD) × Geo. mean of production bin

Table 1

Fraction released to air			
Vap\Sol	<100 mg/L	100-1000	>=1000
<1 Pa	0.004	0.003	0.003
1-10	0.004	0.003	0.003
10-100	0.016	0.007	0.006
100-1000	0.120	0.070	0.021
1000-10000	0.575	0.175	0.085
>10000	**0.825**	0.575	0.175

Table 2

Fraction released to wastewater			
Vap\Sol	<100 mg/L	100-1000	>=1000
<1 Pa	0.11	0.51	**0.76**
1-10	0.11	0.51	0.76
10-100	0.02	0.11	0.51
100-1000	0.01	0.02	0.11
1000-10000	0.01	0.01	0.02
>10000	0.01	0.01	0.01

Table 3

Fraction released to soil			
Vap\Sol	<100	100-1000	>=1000
<1 Pa	**0.0092**	0.0027	0.0004
1-10	0.0092	0.0027	0.0004
10-100	0.0051	0.0011	0.0004
100-1000	0.0011	0.0007	0.0002
1000-10000	0.0004	0.0002	0.0002
>10000	0.0002	0.0002	0.0002

Table 4

Fraction released to the environment (all media)			
Vap\Sol	<100	100-1000	>=1000
<1 Pa	0.12	0.51	0.76
1-10	0.12	0.51	0.76
10-100	0.04	0.11	0.51
100-1000	0.13	0.09	0.13
1000-10000	0.58	0.18	0.10
>10000	0.83	0.58	0.18

Estimating emissions: Tier 2

Batch EU TGD emission model

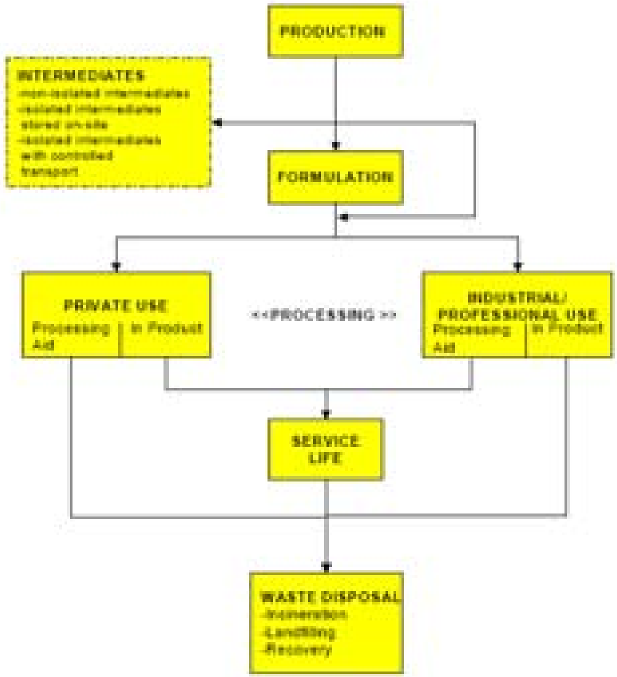


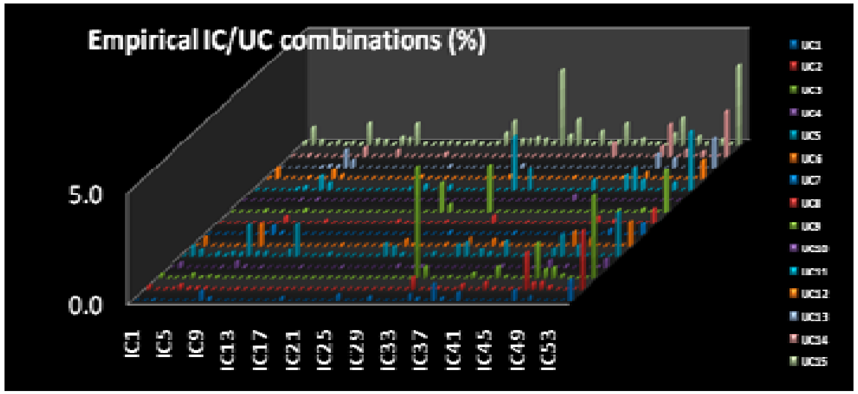
Figure 3 Schematic representation of the life-cycle of a substance

Specific emissions factors based on Industrial Category (IC) and Use Categor (UC) data

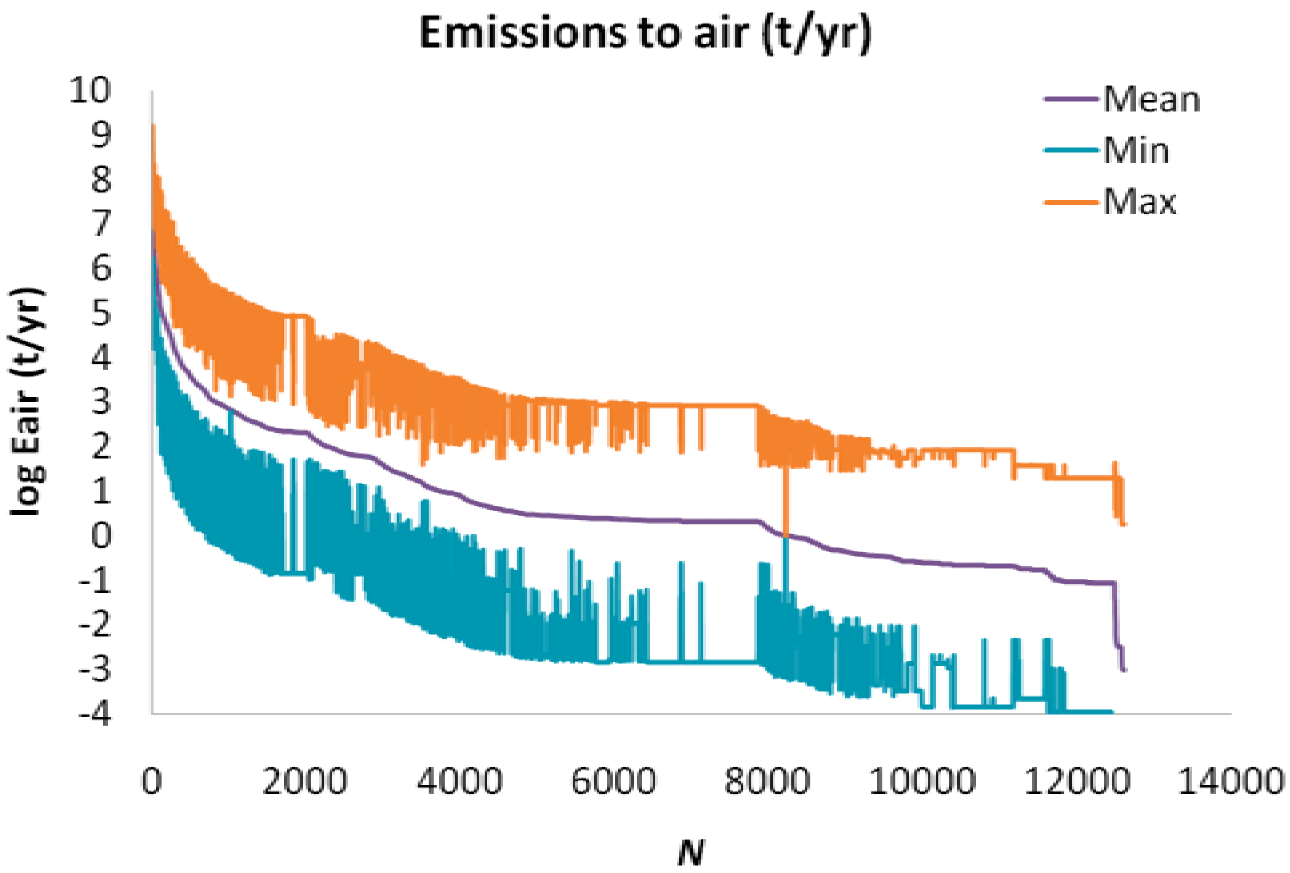
Emissions from various stages of the life-cycle are further distinguished by differences in p/c properties.

Reviewed for ~2800 ESIS chemicals (and very recently, for ~4200 substances included in SPIN (use categories only).

For substances with no information on IC/UC etc, the default profile (fig below) is applied to derive a mean emission estimate.



Estimating emissions to Air



Measured chemical property data availability for organic chemicals on Canada's DSL (~11,300)

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Atmospheric reaction half-lives ~4%

Water and soil half-lives = 12 chemicals!

Lab tests of chemical degradation <7%

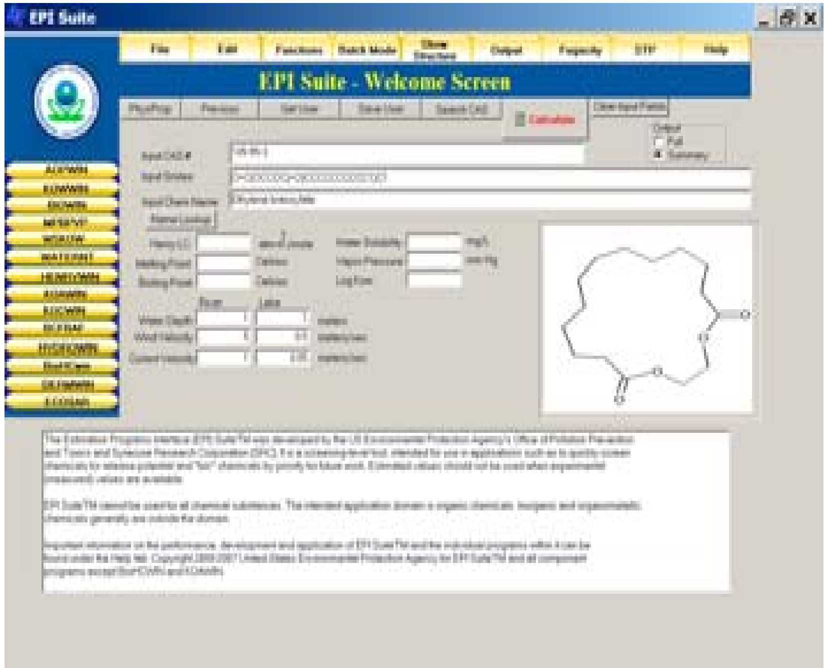
Lab BCF data in fish, i.e., no dietary uptake, <4%

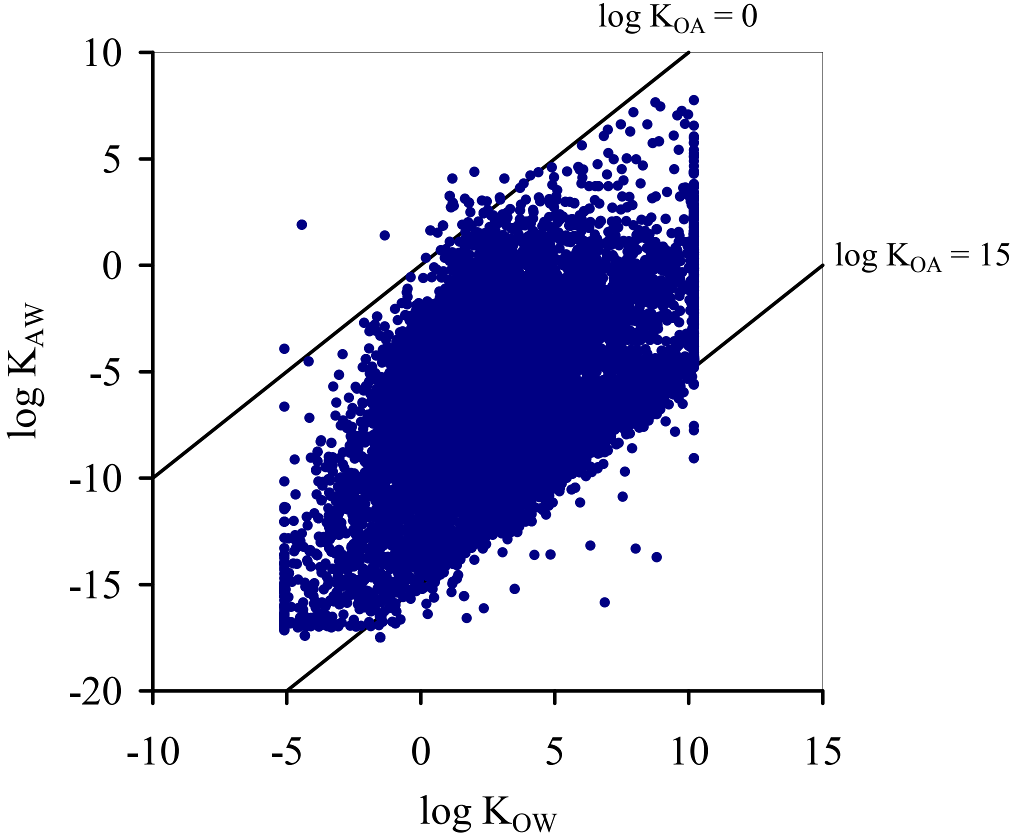
Physical-chemical properties

Vapour pressure <5%; Aqueous solubility <5%; K_{OW} <10%

Partitioning properties and multimedia half-lives

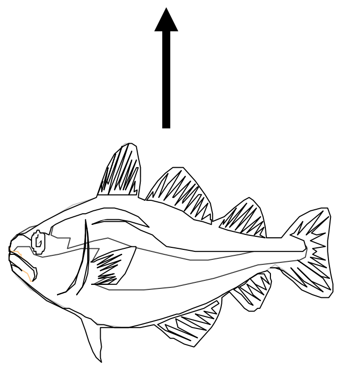
n ~13,000

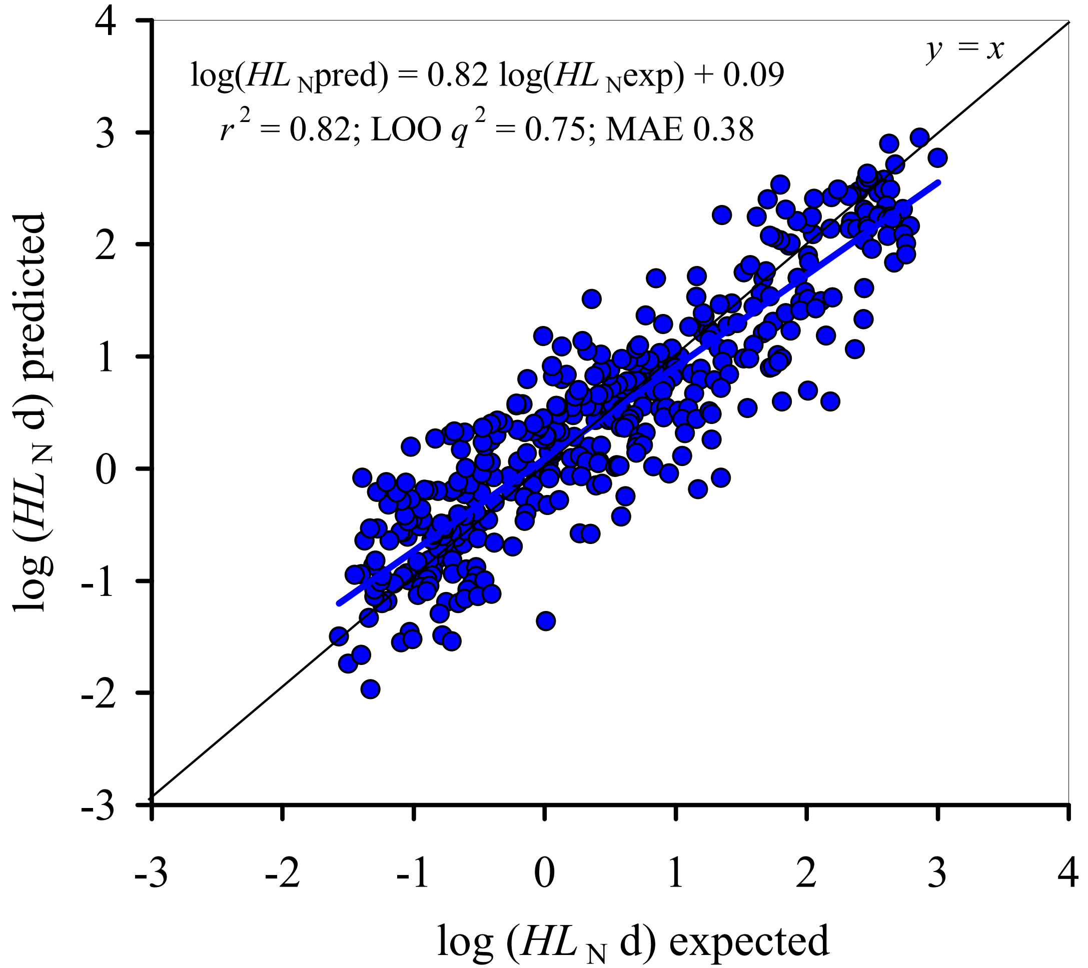




Biotransformation half-life predictions

Metabolic biotransformation
HL in fish using a QSAR





Environ Toxicol Chem 28, 1168 - 1177

Biotransformation half-life predictions

Stockholm University

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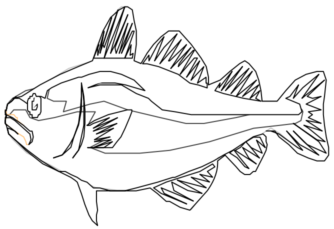
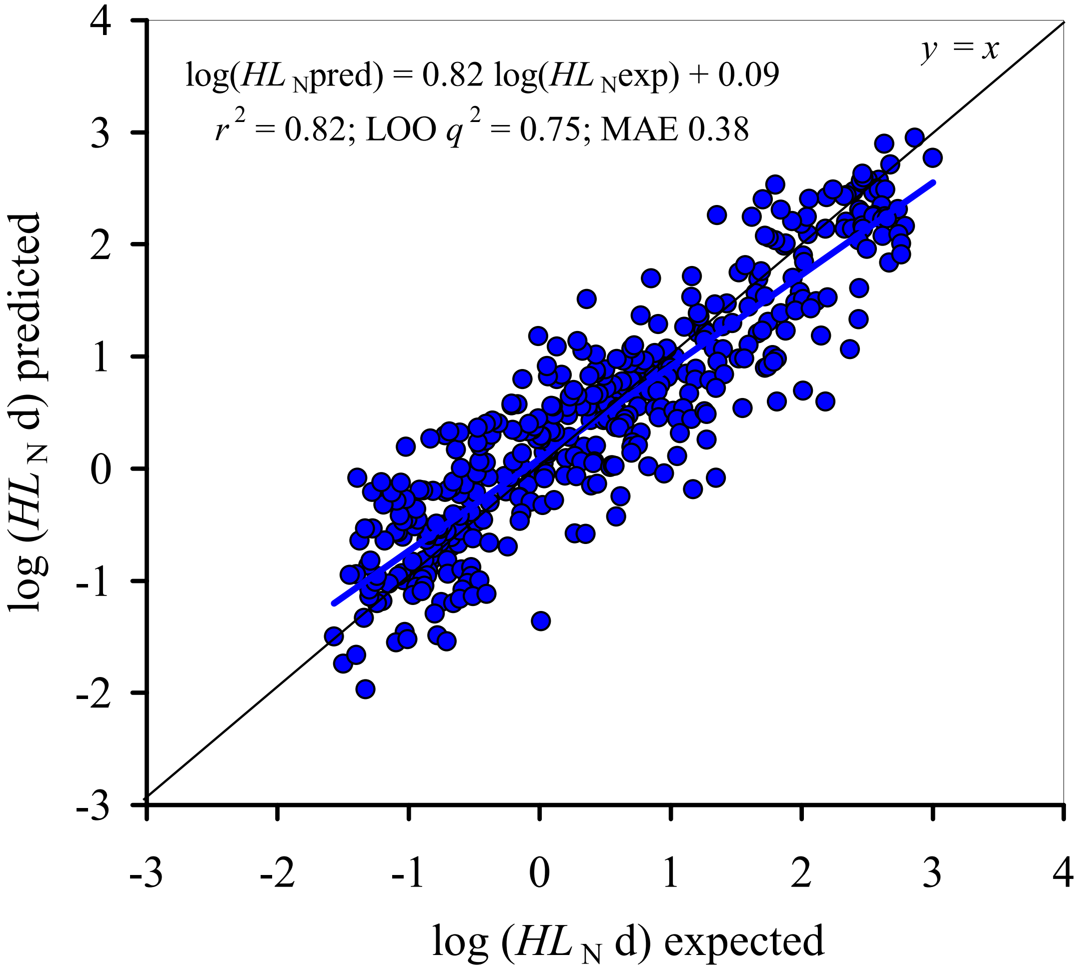
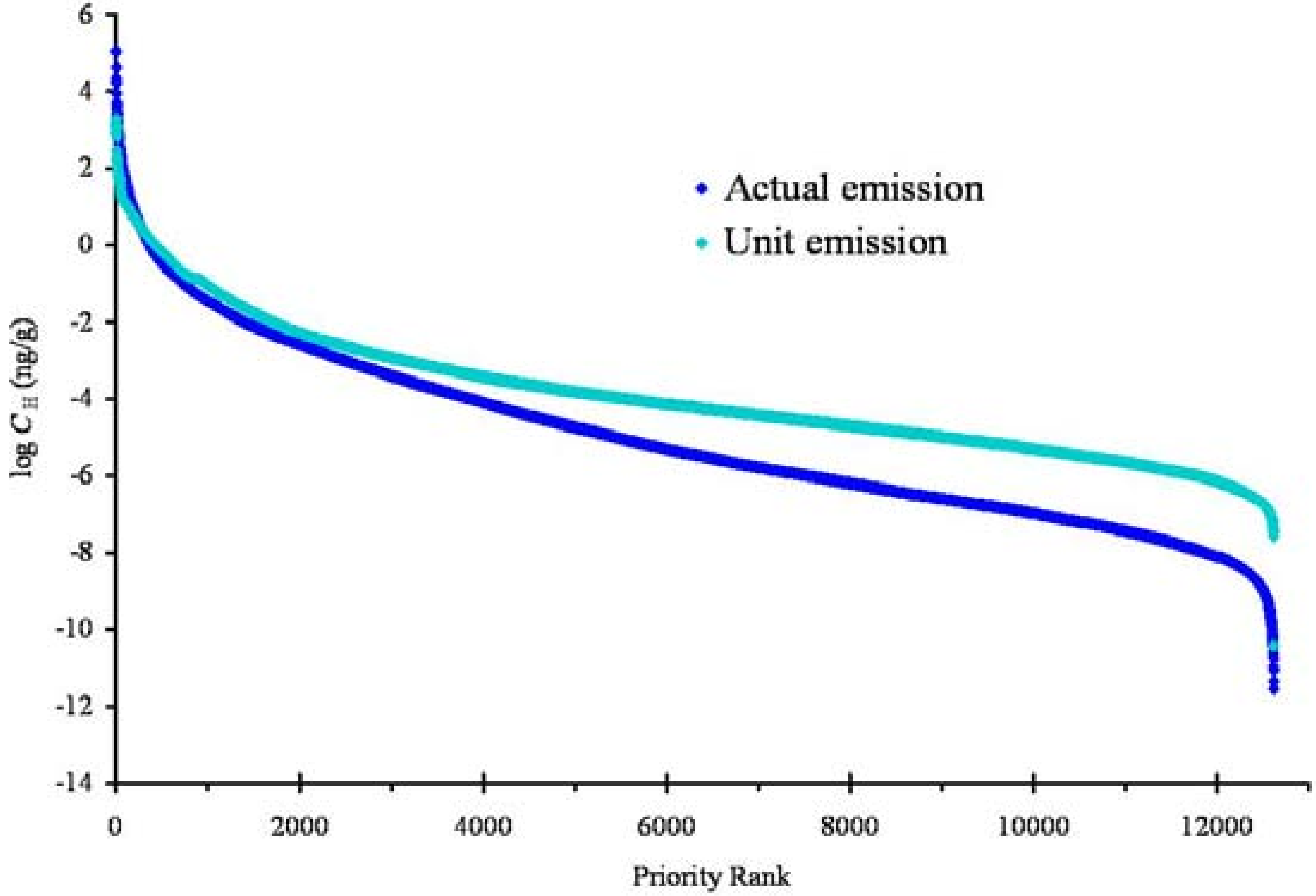


Need to extrapolate fish data to other vertebrates because QSARs are not currently available

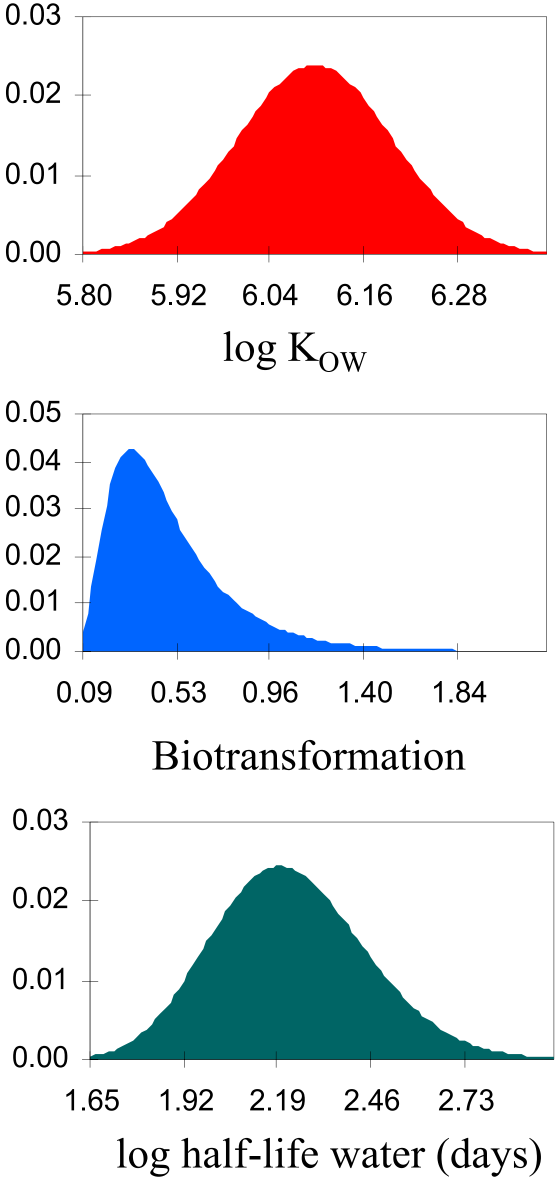


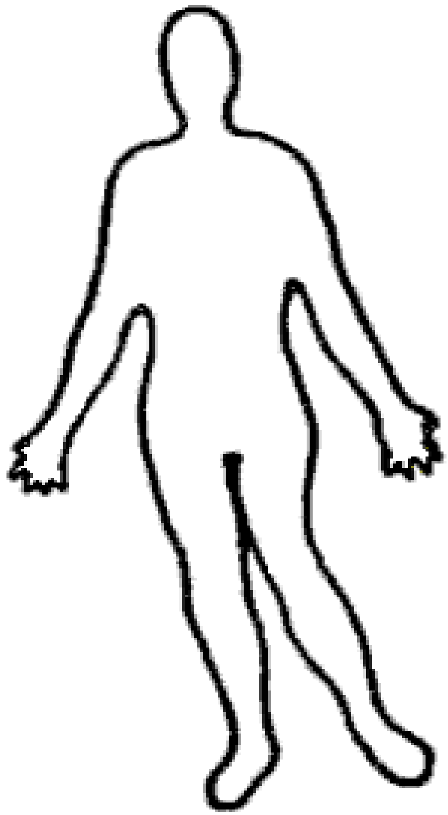
Environ Toxicol Chem 28, 1168 - 1177

Initial ranking of industrial chemicals according to human exposure



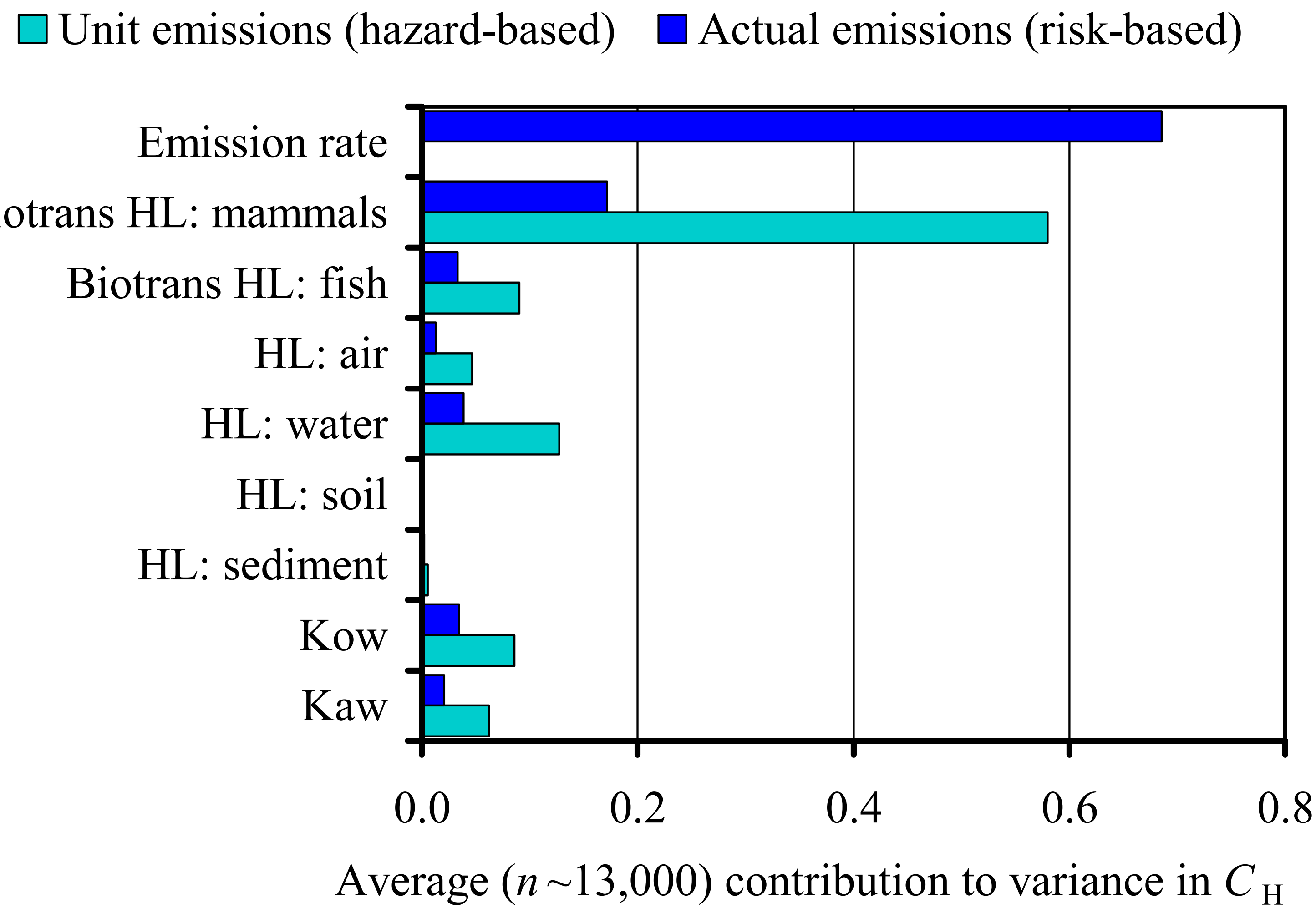
Identifying the sources of uncertainty





Propagation of uncertainty in C_H

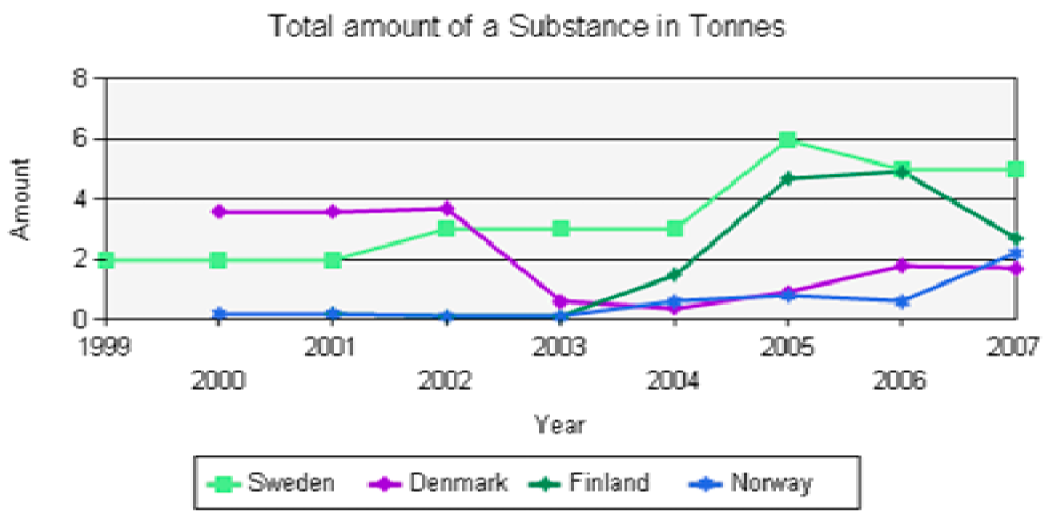
Sources of uncertainty in predicted exposure of humans to industrial chemicals



Ongoing work: Emissions estimates

Search for more in-depth information on short-listed chemicals (e.g. Use categories) through various database (e.g. SPIN) and literature searches.

Cross-check emission estimates with complementary outputs from the Exposure Index



Thanks to Stellan Fischer (KEMI) and Jan Kraft (KLIF) for support (Exposure Index and SPIN)

Ongoing work: Biotransformation

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METABOLIC BIOTRANSFORMATION IN FISH: A QSAR APPROACH

Ester Papa[a], Alessandra Mozzi[a], Paola Gramatica[a], Jon A. Arnot[b], Don Mackay[c]
[a]QSAR Research Unit in Environmental Chemistry and Ecotoxicology, DBSF, University of Insubria, Varese (Italy); [b] Department of Physical and Environmental Science, University of Toronto Scarborough, Toronto, ON (Canada); [c] The Canadian Centre for Environmental Modelling and Chemistry, Trent University, Peterborough, ON (Canada)
E-mail: ester.papa@uninsubria.it

SETAC North America's 30th Anniversary in New Orleans 19-23 November, 2009

QSAR model for predicting rate of metabolism in fish

Ovanes Mekenyan, Sabcho Dimitrov, Nadezhda Dimitrova
Laboratory of Mathematical Chemistry, University "Prof. As. Zlatarov", Bourgas, Bulgaria
Jon Arnot
Center for environmental, modeling and Chemistry, Trent University, Ontario, Canada
Mark Bonnell
New Chemicals Evaluation Unit at Environment Canada, Ottawa, Canada
Thomas Parkerton
Toxicology & Environmental Science Division ExxonMobil Biomedical, Sciences Inc., Annandale, NJ

Prediction of Metabolic Biotransformation Half-Lives Using Iterative Fragment Selection (IFS)

Trevor N. Brown, Jon Arnot, Frank Wania
Department of Chemistry, Department of Physical and Environmental Sciences
University of Toronto Scarborough, Canada

Working with the results:
Sieving for possible unknown contaminants

Stockholm University

Starting with the **Tier 1** results,

identify and disregard:

- known POPs, e.g. PAHs
- apparent "non-POPs", e.g. alkanes, sugars
- likely "non-POPs", e.g. reactive compounds/precursors

Reveals further weaknesses:

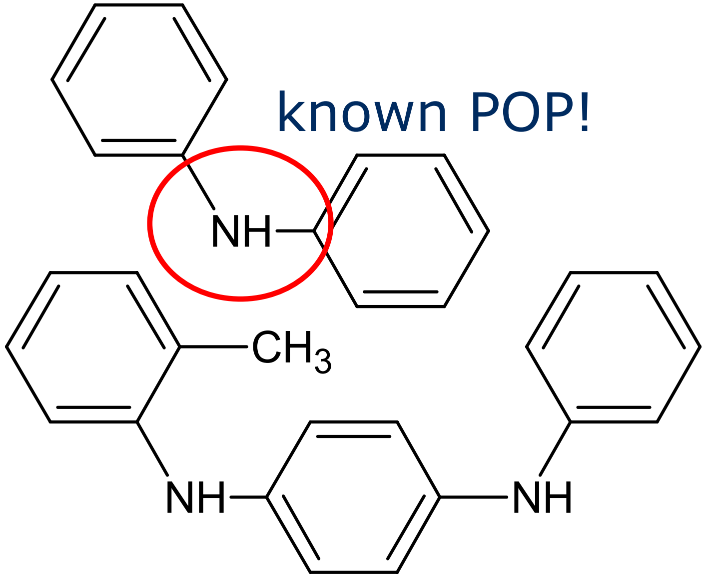
- prediction of hydrolysis (no QSAR)
- dissociating chemicals
- heterogeneity in emissions

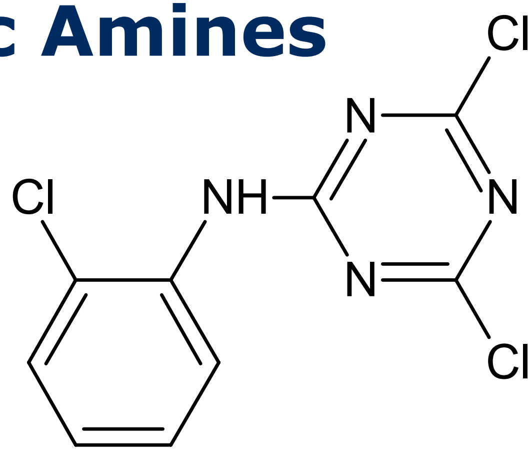
Working with the results:
Developing sampling and method development strategies

The model helps us:

- Choose relevant matrices
- Choose sampling sites
- Choose time scale of sampling
- Set a target limit of quantification for the analytical method

Group 1: Aromatic Amines





analysis by: HPLC-MS/MS

compartment: water / sediment

usage: antioxidant (rubber, plastics, textiles, gunpowder, …)

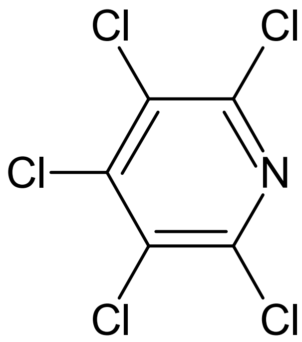
14 compounds

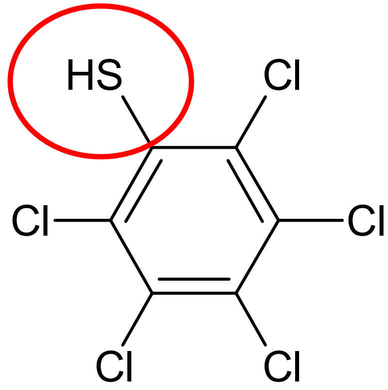
potentially charged at the amine group

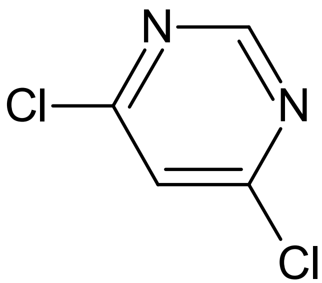
⇒ estimate pK_a (SPARC, SciFinder [ACDLabs])

⇒ all except 1 (cationic) are neutral

Group 2: Halogenated Heterocycles







analysis by: GC-MS

compartment: air

usage: mainly intermediates

6 compounds

neutral except 1 (anionic)

photolysis?

Future work:
Evaluation of the screening system

- Compare the ranking with existing measured concentrations in humans and the environment, both from the literature and from the project

Conclusions

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- Exposure modeling can now be used for high throughput screening of industrial chemicals

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- This is useful for selecting chemicals for screening
- Still a ways to go before we have a robust and accurate tool
- But the science is developing quickly!

Acknowledgements

Stockholm University

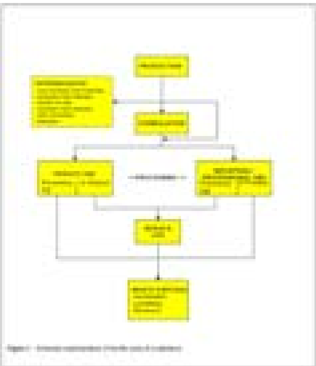
Cefic Long-range Research Initiative (LRI)
for funding

cefic LRI
The Long-range
Research initiative

Emissions: Discussion

- Data on production, import, use and releases of industrial chemicals are difficult to access / confidential.
- Development of reliable emission scenarios thus represent a major challenge, in part because of confidentiality issues concerning relevant data (e.g. Industrial Category, Use Categories etc) and comparability of data (i.e. different reporting requirements etc.).

Existing Methods (EU TGD)



EUROPEAN COMMISSION
JOINT RESEARCH CENTRE
Institute for Health and Consumer Protection
European Chemicals Bureau

Public Availability of Data on
EU High Production Volume Chemic

TABLE 1. IUCLID chapters and sub-chapters: Producer Related Part (Chapter 1)

Chapter	Chapter Description	Availability
1	**General Information**	
1.1*	General Substance Information	99.63%
1.2	Synonyms	94.20%
1.3*	Impurities	71.85%
1.4*	Additives	45.40%
1.5*	Quantity	100.00%
1.6.1*	Labelling	97.93%
1.6.2*	Classification	97.36%
1.7*	Use Pattern	99.59%
1.8	Occupational Exposure Limit Value	76.15%
1.9*	Source of Exposure	67.14%
1.10	Water Pollution	41.74%
1.11	Major Accident Hazards	33.59%
1.12	Air Pollution	25.72%
1.13*	Additional Remarks	55.01%

Parts of the information in the "*" marked sub-chapters are currently regarded as confidential, but disclosure may be done in the future.

CHAPTER 1 **General Information**

	1.1	1.2	1.3	1.4	1.5	1.6.1	1.6.2	1.7	1.8	1.9	1.10	1.11	1.12	1.13	Chapter
RECORDS	13,490	44,055	14,289	4,0[illegible]8	19,029	13,823	19,577	52,044	11,125	6,089	2,294	1,893	1,382	5,230	208,408
SUBS. WITH RELEVANT RECORDS	2,456 99.63%	2,322 94.20%	1,771 71.85%	1,119 45.40%	2,465 100.00%	2,414 97.93%	2,400 97.36%	2,455 99.59%	1,877 76.15%	1,655 67.14%	1,029 41.74%	828 33.59%	634 25.72%	1,356 55.01%	2,465 100.00%
SUBST. WITHOUT RELEVANT RECORDS	9	143	694	1,346	0	51	65	10	588	810	1,436	1,637	1,831	1,109	0

On average ~7 records on quantity per HPVCs