Understanding the ecotoxicological risks of ionic liquids - where are we?

Green Solvents for Processes

Friedrichshafen/Germany

October 8-11, 2006.

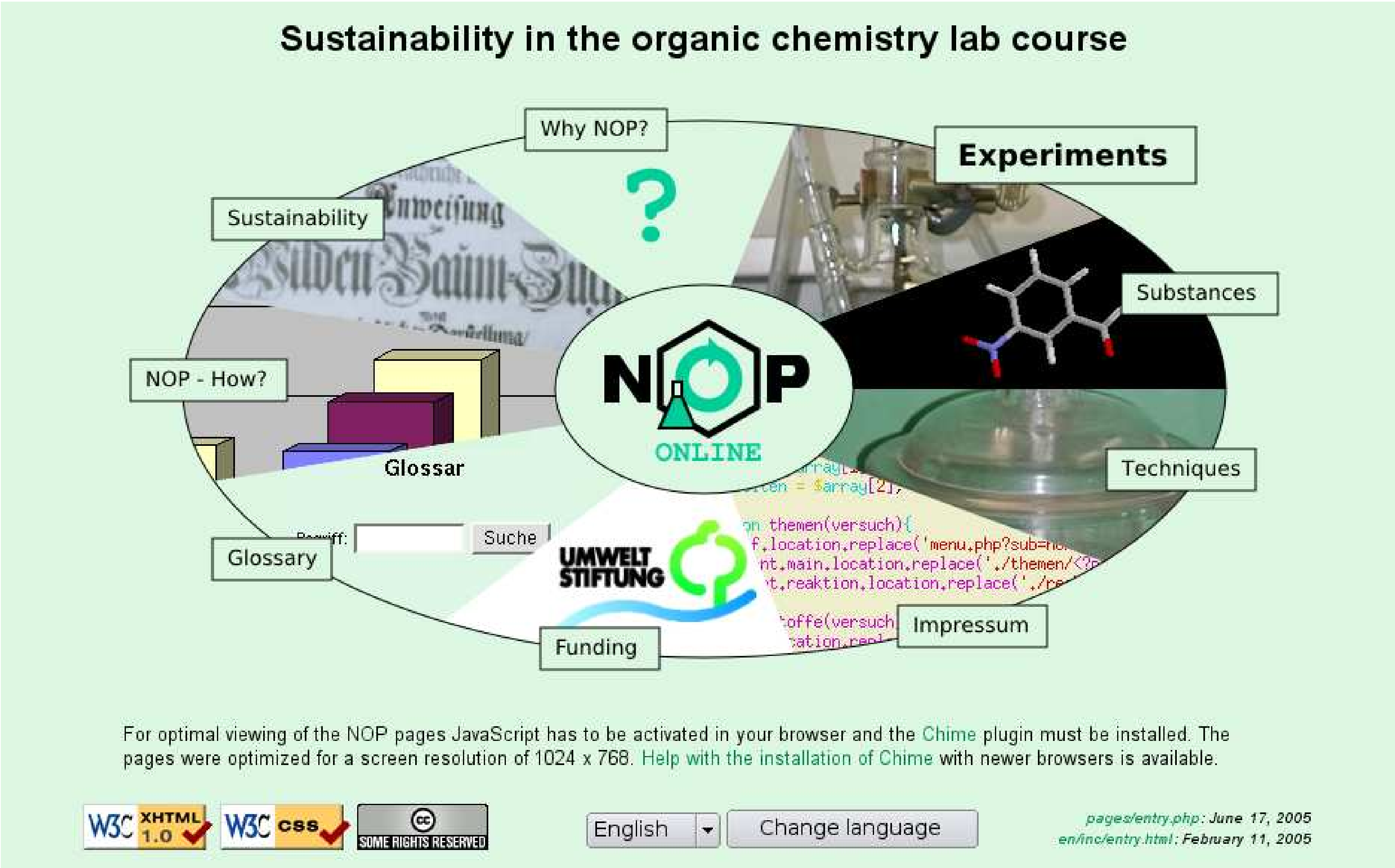
J. Ranke, J. Arning, P. Behrend, A. Böschen, U. Bottin-Weber, J. Filser, T. Juffernholz, M. Matzke, A. Müller, M. Schaefer, S. Stolte, R. Störmann, K. Thiele, J. Thöming, B. Jastorff

University of Bremen/D

Universität Bremen

UFT

www.oc-praktikum.de



The UFT

Chemical Engineering
Regeneration & Recycling
Prof. Thöming

Biotechnology
Prof. Blohm

Molecular Genetics
Prof. Becker

Environmental
Process Engineering
Prof. Räbiger

UFT
Zentrum für
Umweltforschung und
Umwelttechnologie

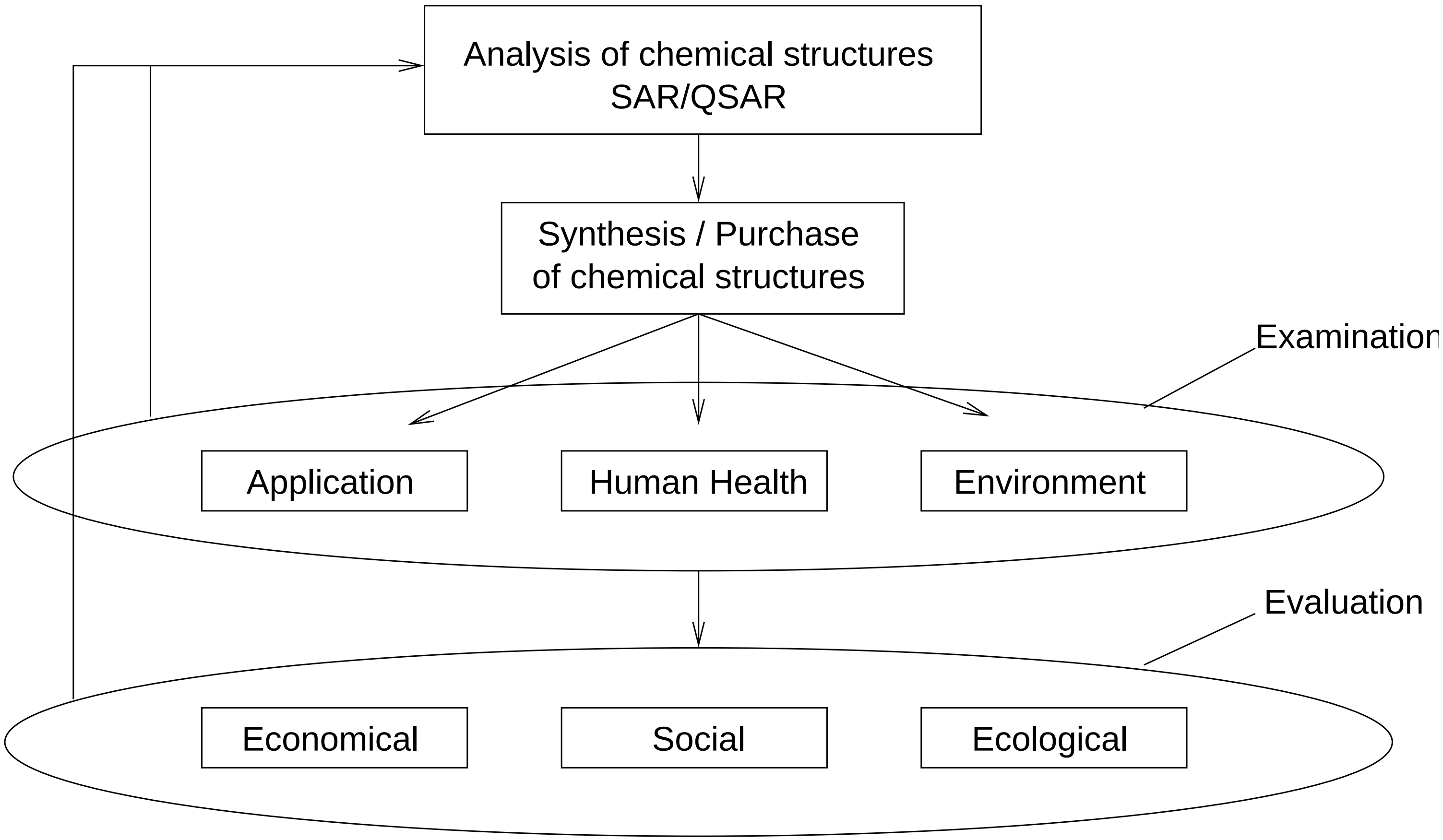
Ecology
Prof. Filser

Physiogeography
Prof. Venzke

Bioorganic Chemistry
Prof. Jastorff

The UFT IL team

Sustainable Product Design



Technosphere vs. Environment

	Technosphere	Environment
Degree of control	high	low
Degree of knowledge	high	low

Uncertainty and Ignorance

Chemistry dealing with biological and environmental systems has to deal with

- more complexity

Uncertainty and Ignorance

Chemistry dealing with biological and environmental systems has to deal with

- more complexity
- more uncertainty

Uncertainty and Ignorance

Chemistry dealing with biological and environmental systems has to deal with

- more complexity
- more uncertainty
- more ignorance

Green and sustainable chemistry

includes both technospheric and environmental chemistry:

Green and sustainable chemistry

includes both technospheric and environmental chemistry:

$\Rightarrow$ High standards of deterministic knowledge in technospheric area

Green and sustainable chemistry

includes both technospheric and environmental chemistry:

$\Rightarrow$ High standards of deterministic knowledge in technospheric area

$\Rightarrow$ Great efforts to deal with uncertainty in environmental area

Green and sustainable chemistry

includes both technospheric and environmental chemistry:

⇒ High standards of deterministic knowledge in technospheric area

⇒ Great efforts to deal with uncertainty in environmental area

⇒ *Understanding* ecotoxicological risks

Elements of ecotoxicological risks

Five risk indicators

Technosphere

Environment

Ranke J (2001) PhD Dissertation

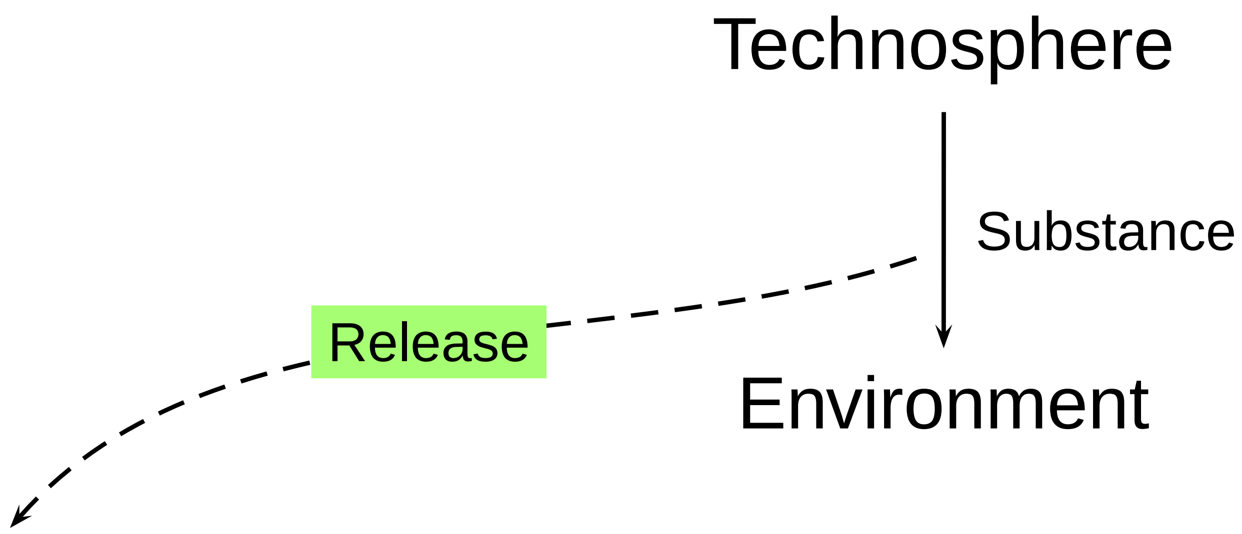
Five risk indicators

Technosphere

↓ Substance

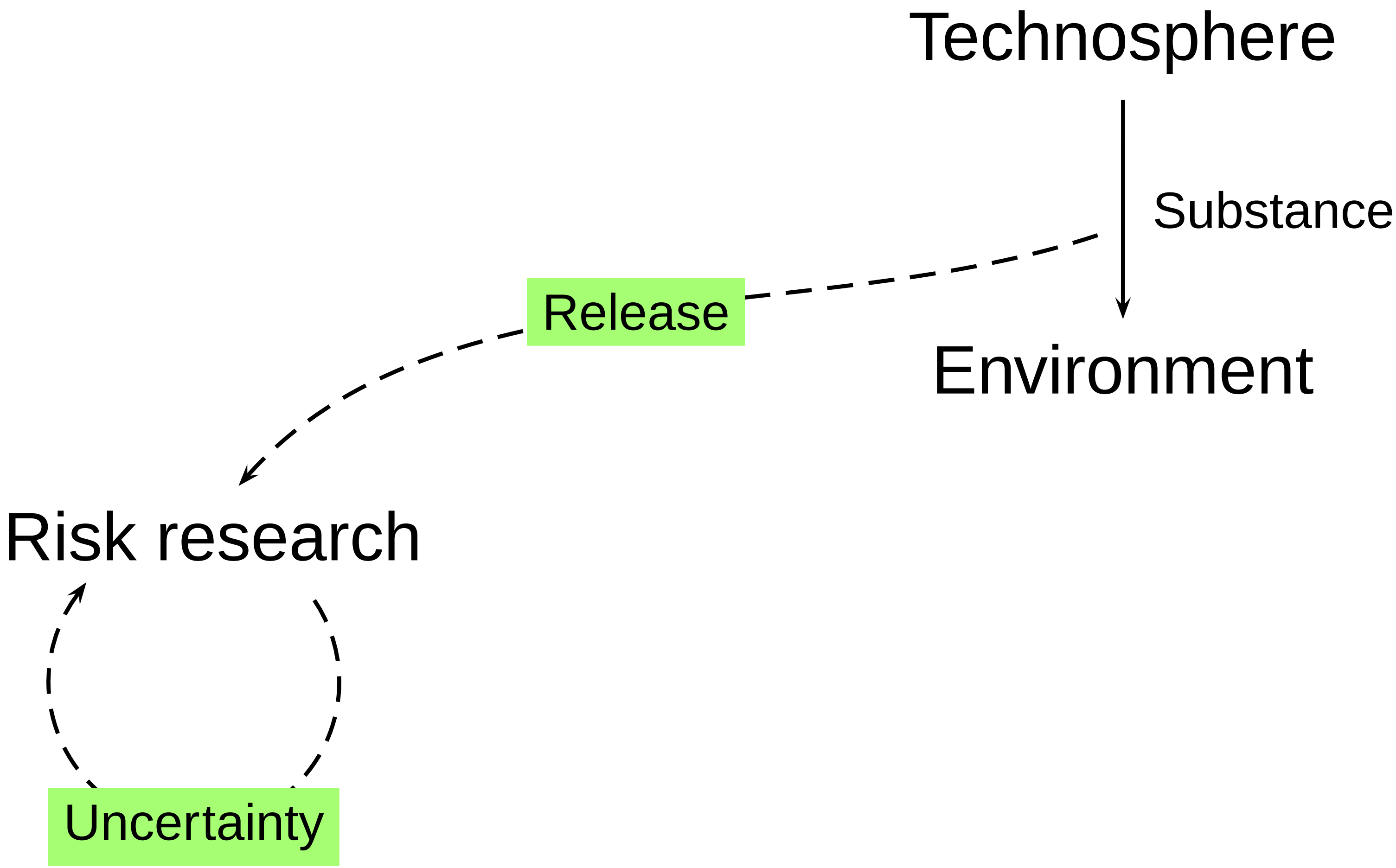
Environment

Five risk indicators

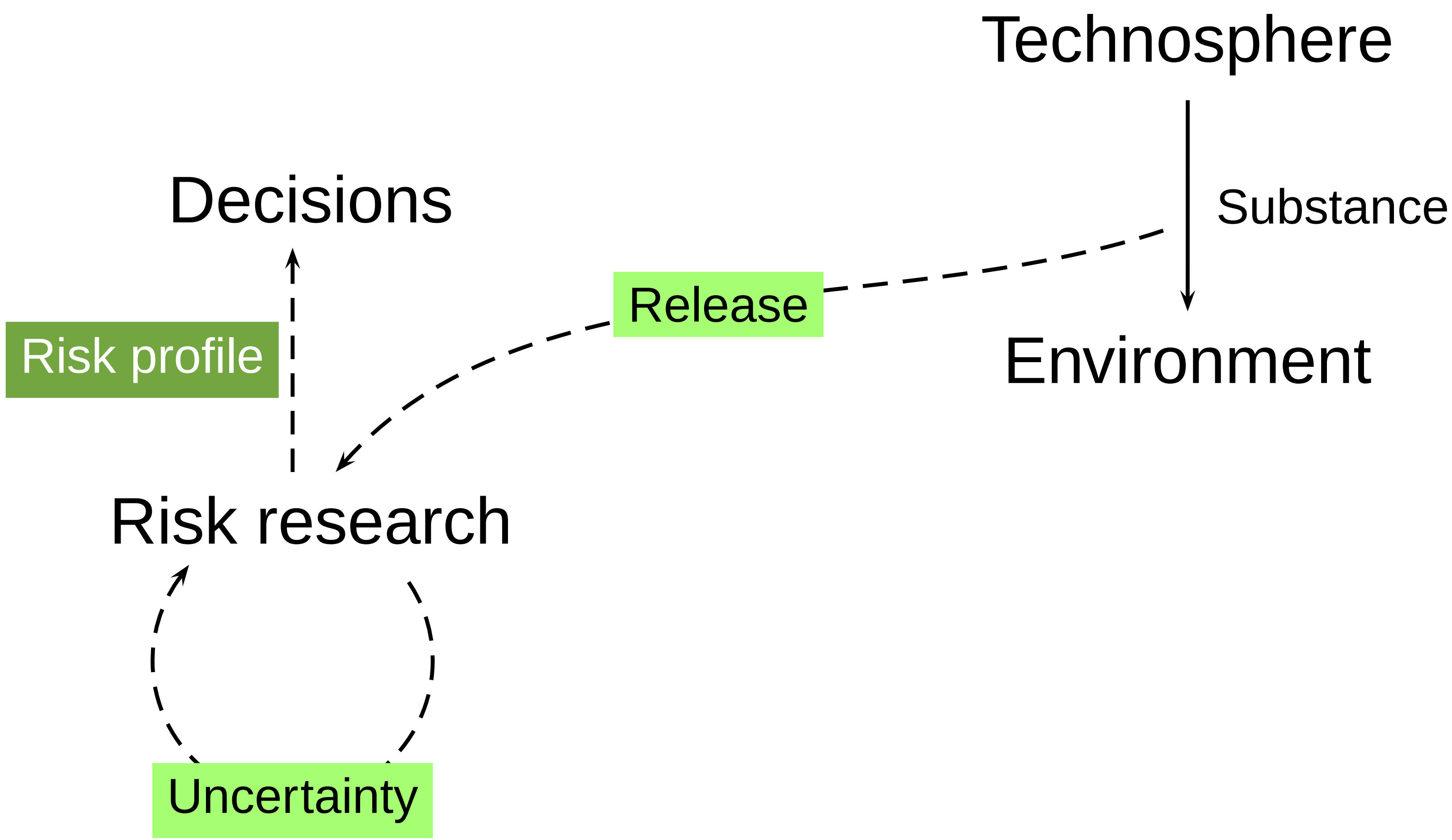


Ranke J (2001) PhD Dissertation

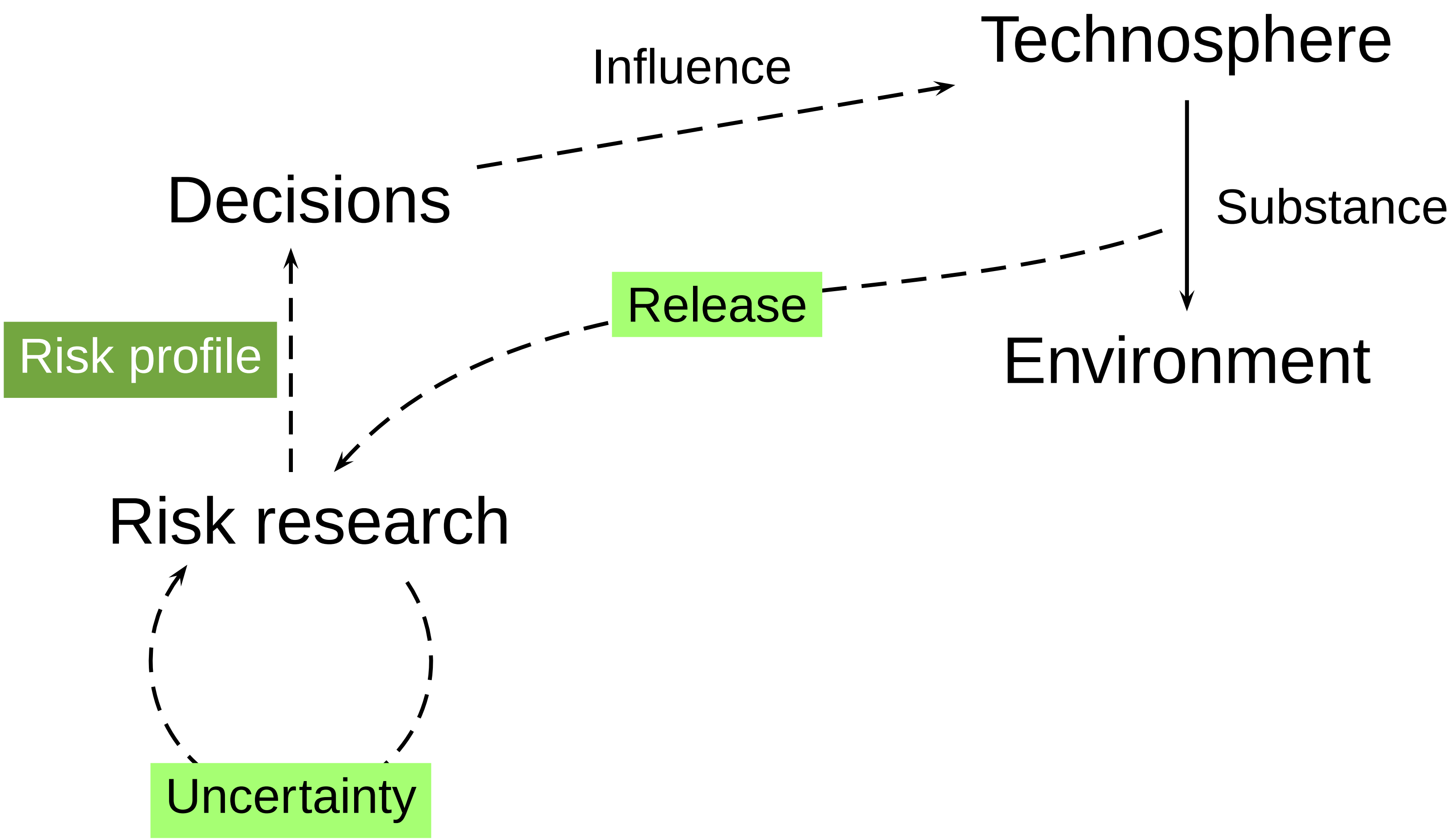
Five risk indicators



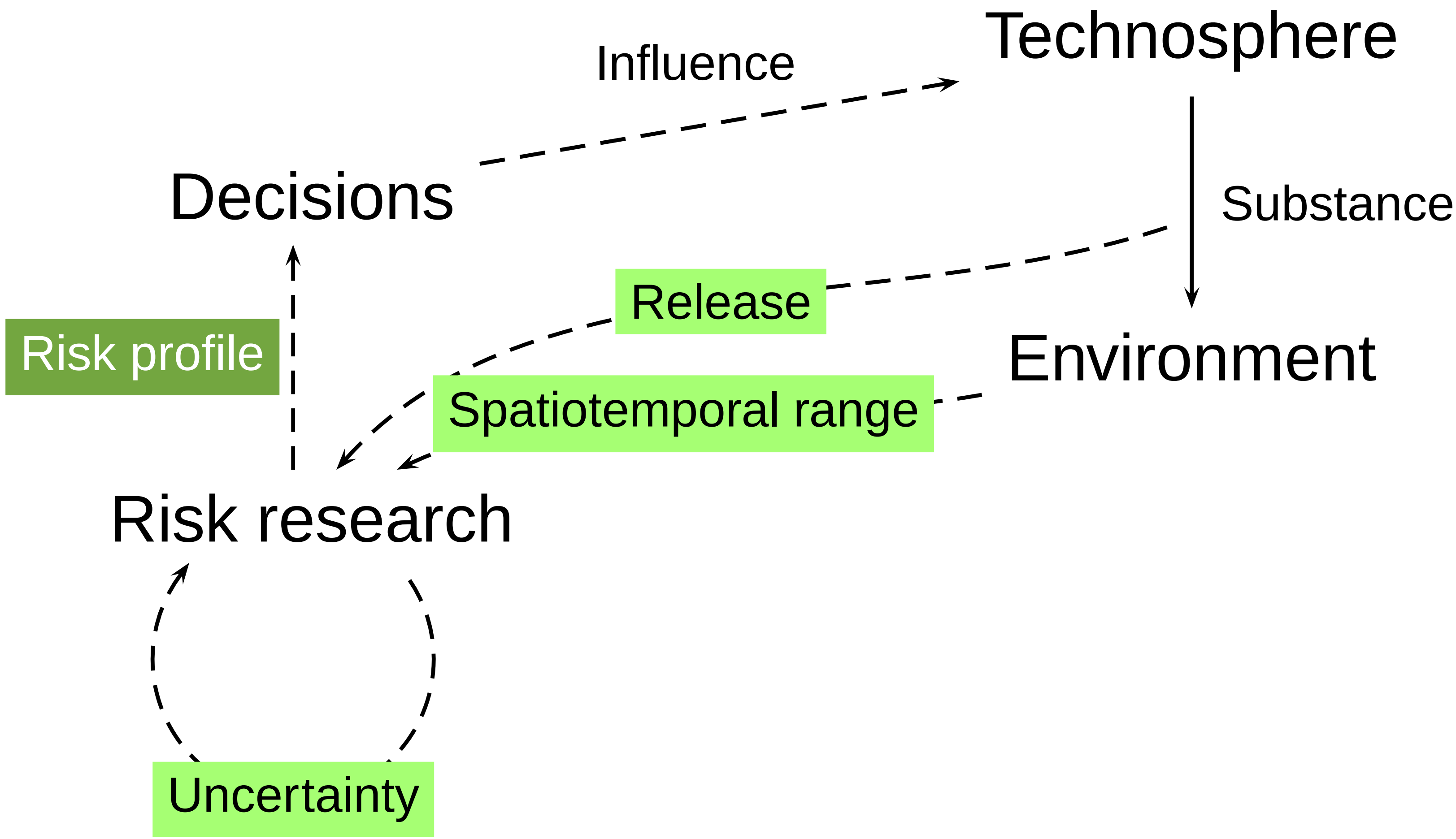
Five risk indicators



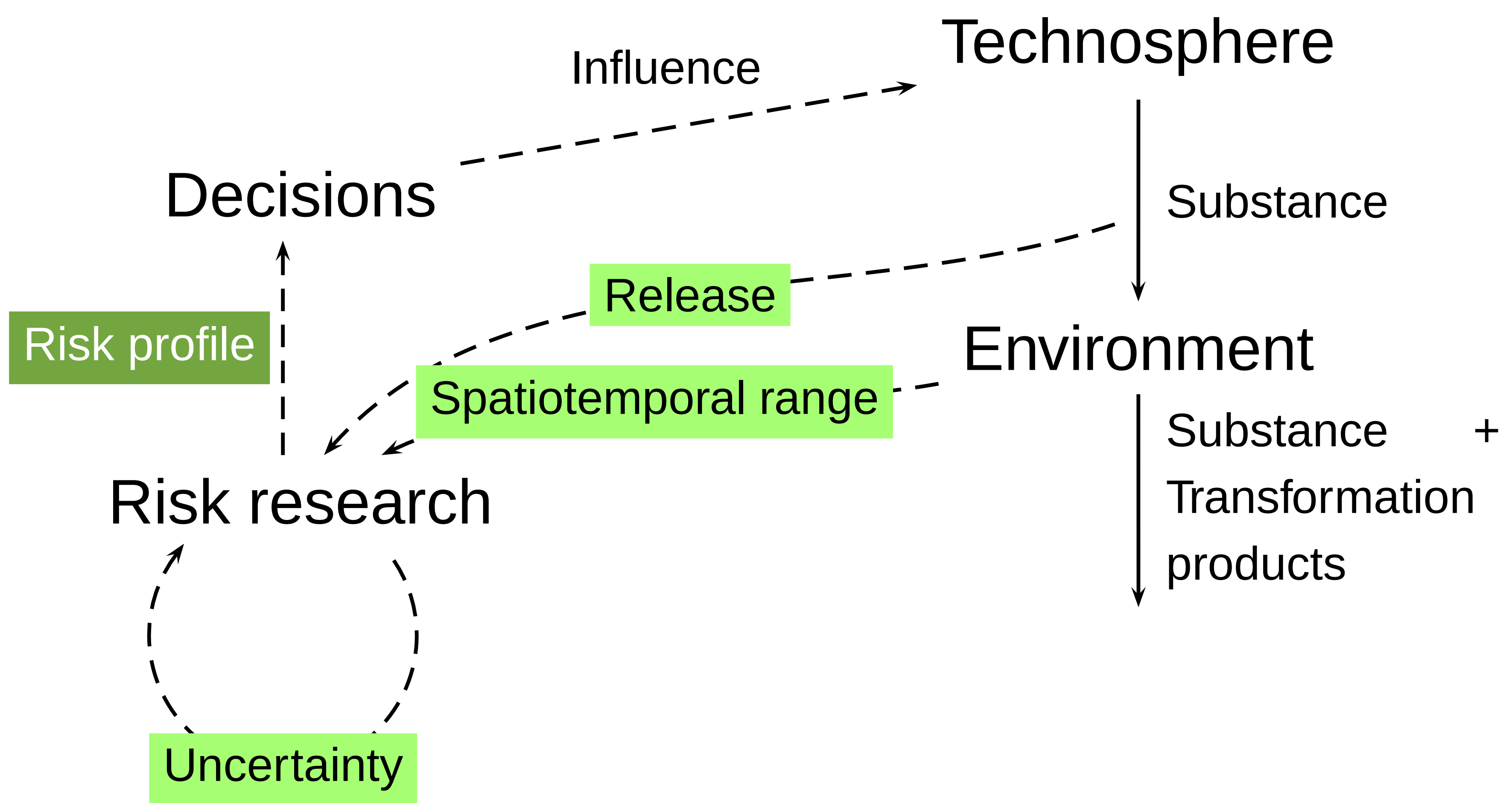
Five risk indicators



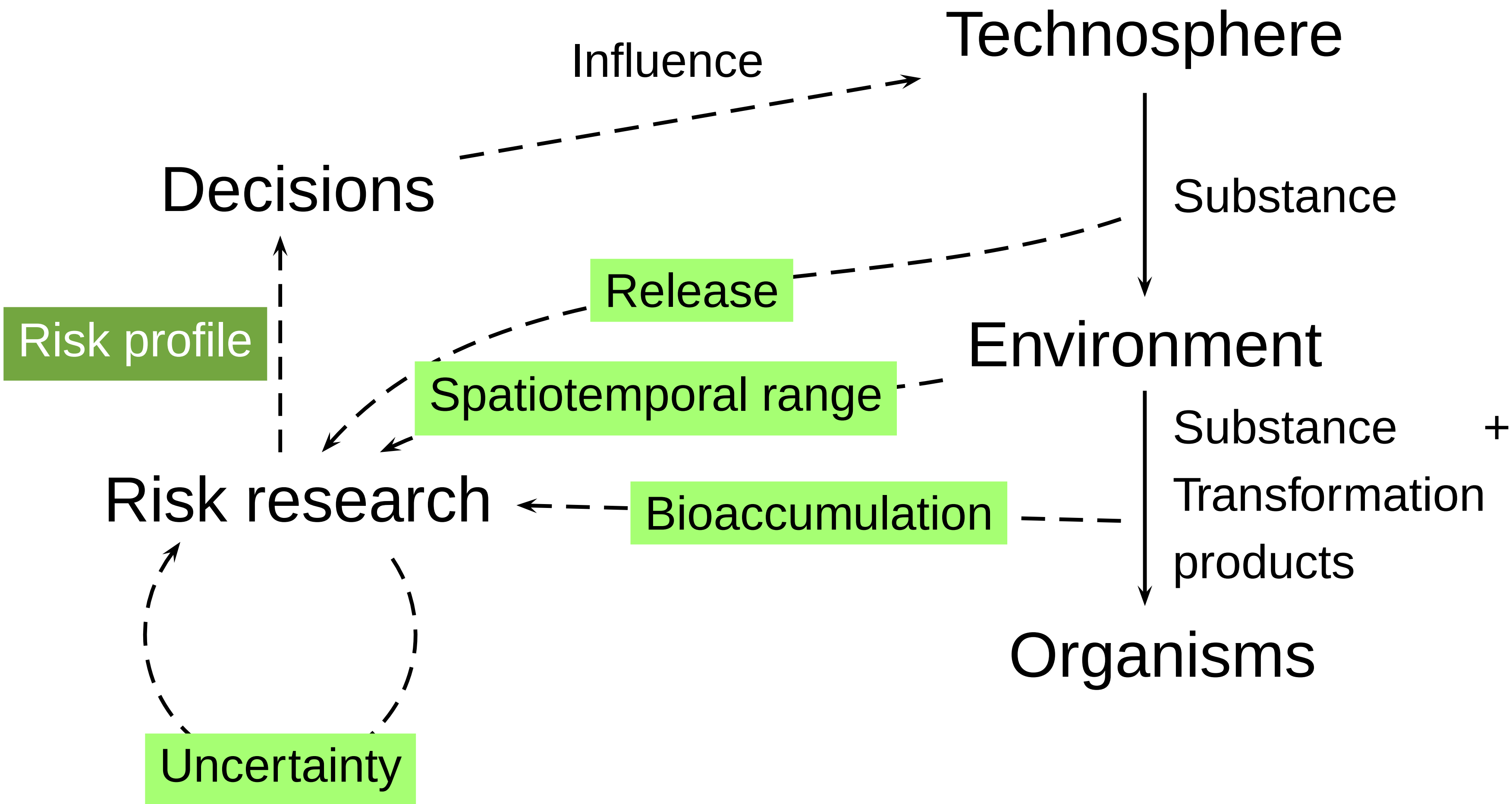
Five risk indicators



Five risk indicators

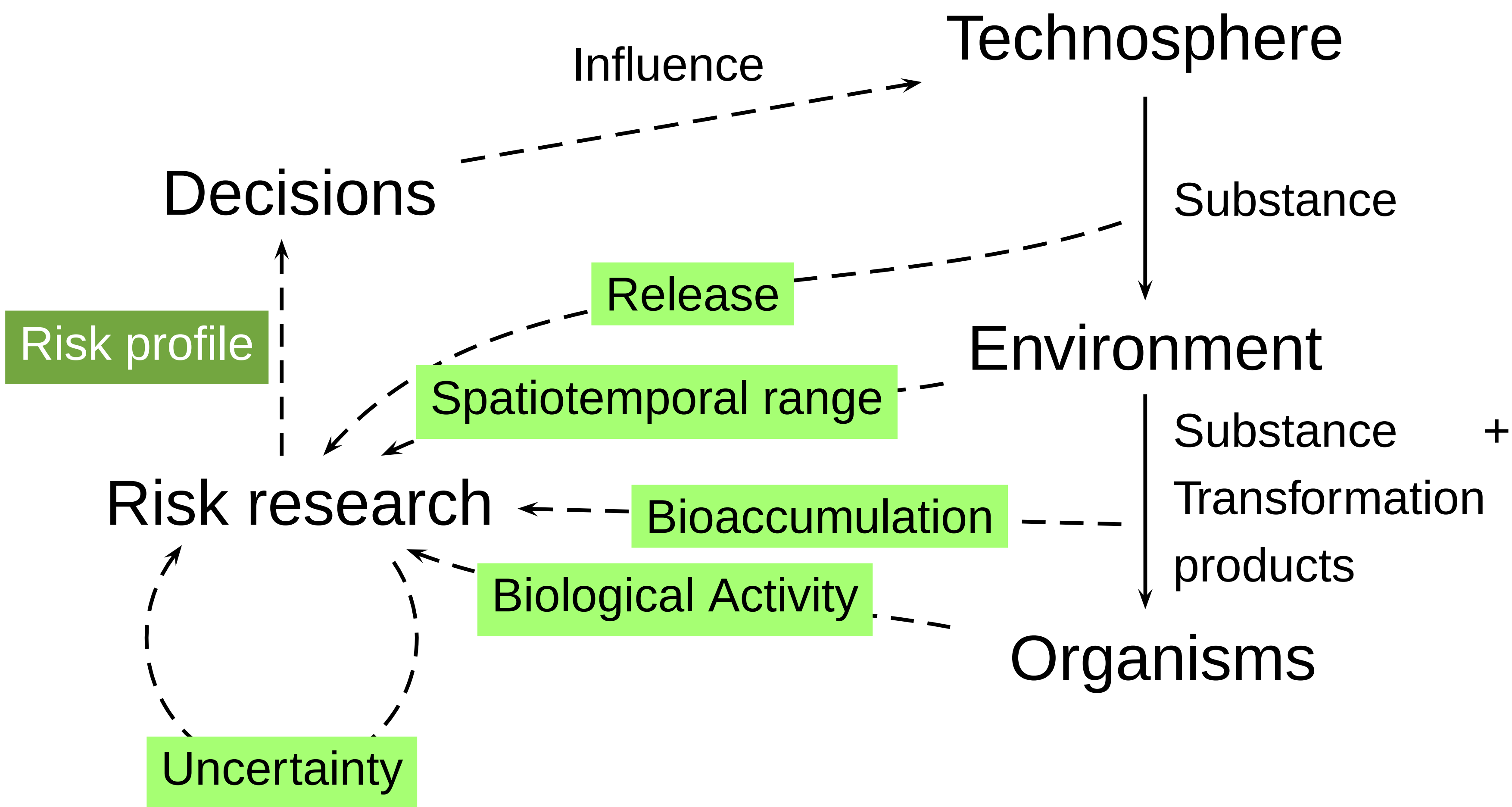


Five risk indicators



Ranke J (2001) PhD Dissertation

Five risk indicators



Release of ionic liquids

- Gaseous release (impurities, decomposition products)

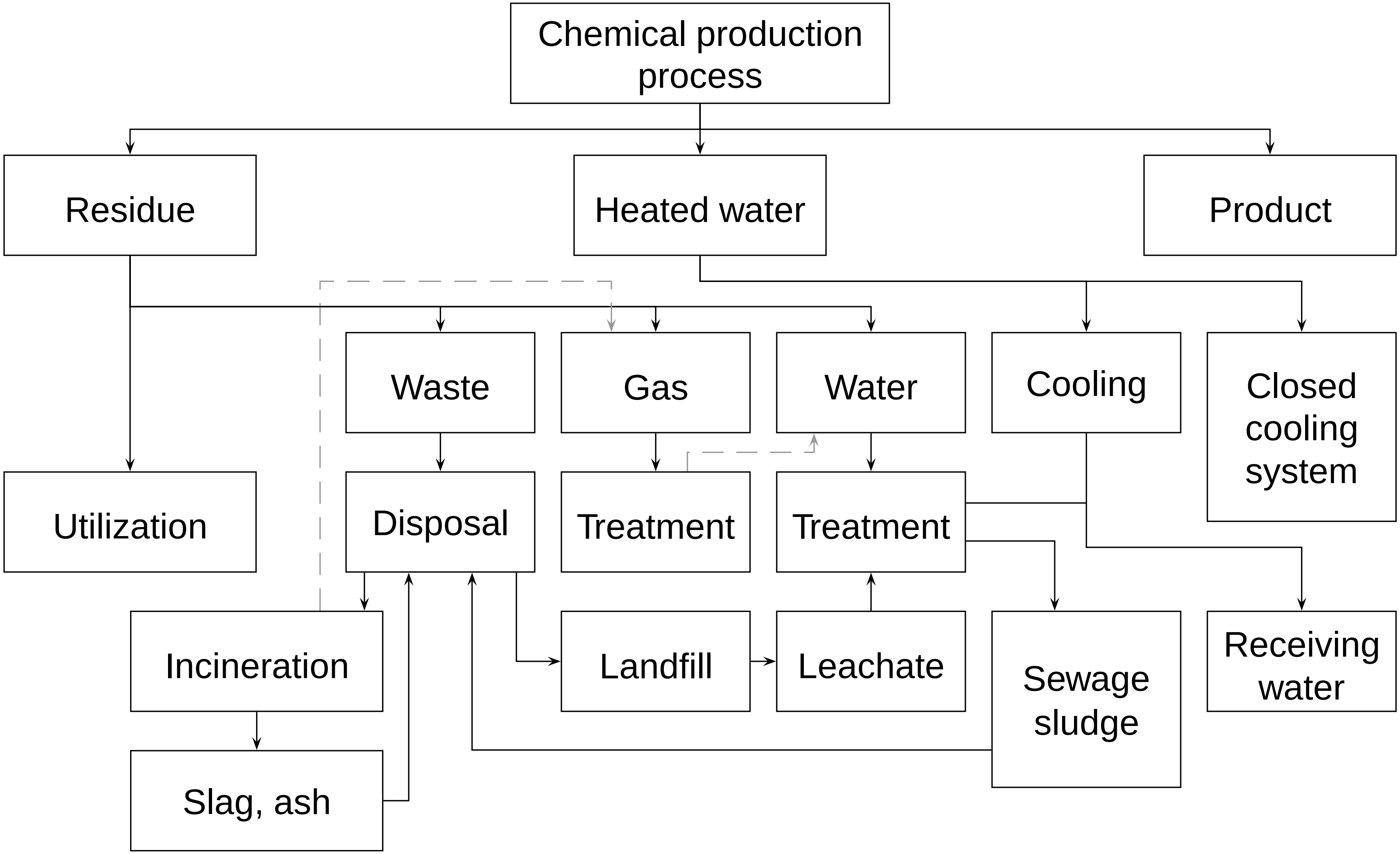
Release of ionic liquids

- Gaseous release (impurities, decomposition products)
- Waste water

Release of ionic liquids

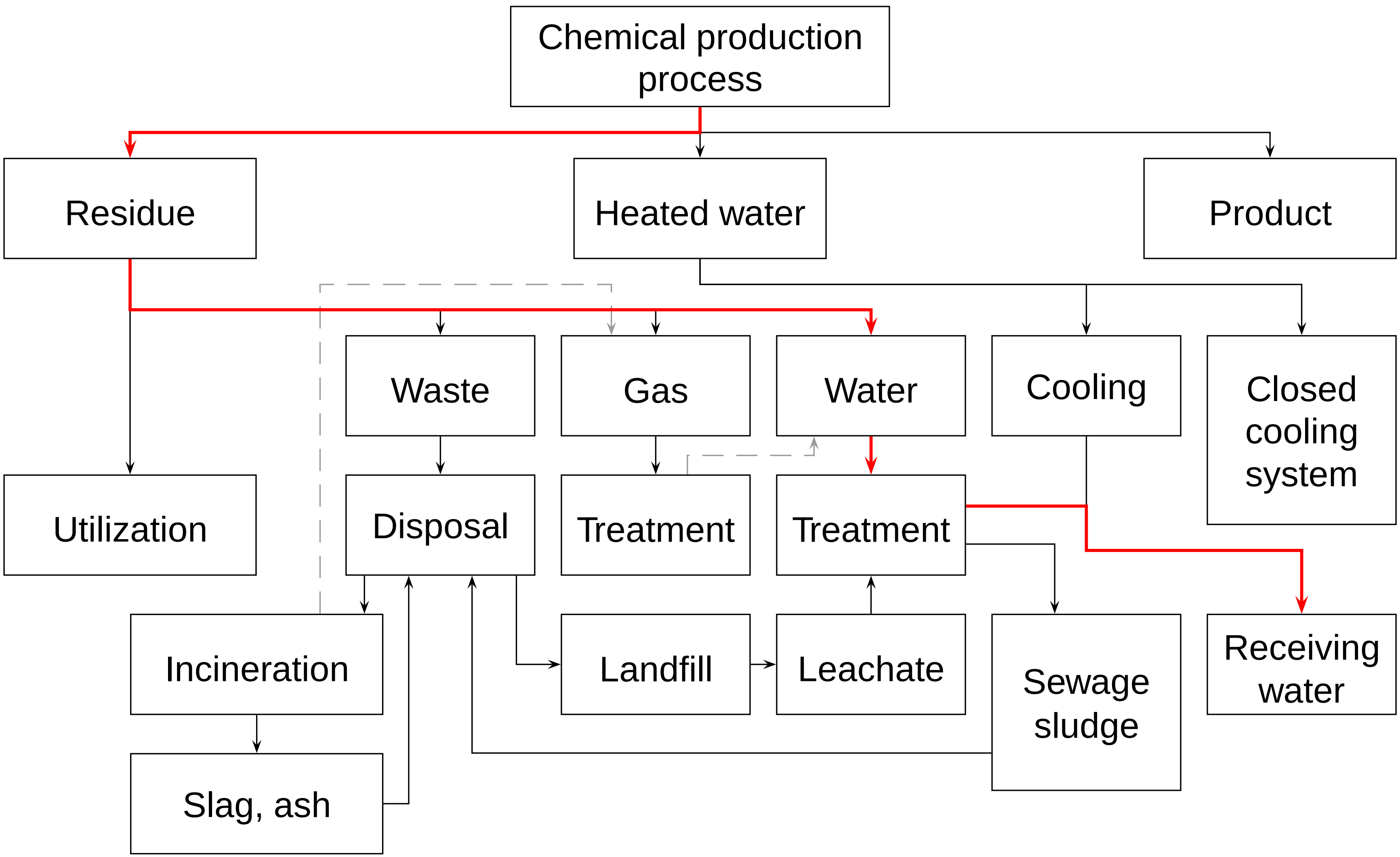
- Gaseous release (impurities, decomposition products)
- Waste water
- Accidental releases to soil or water

Release



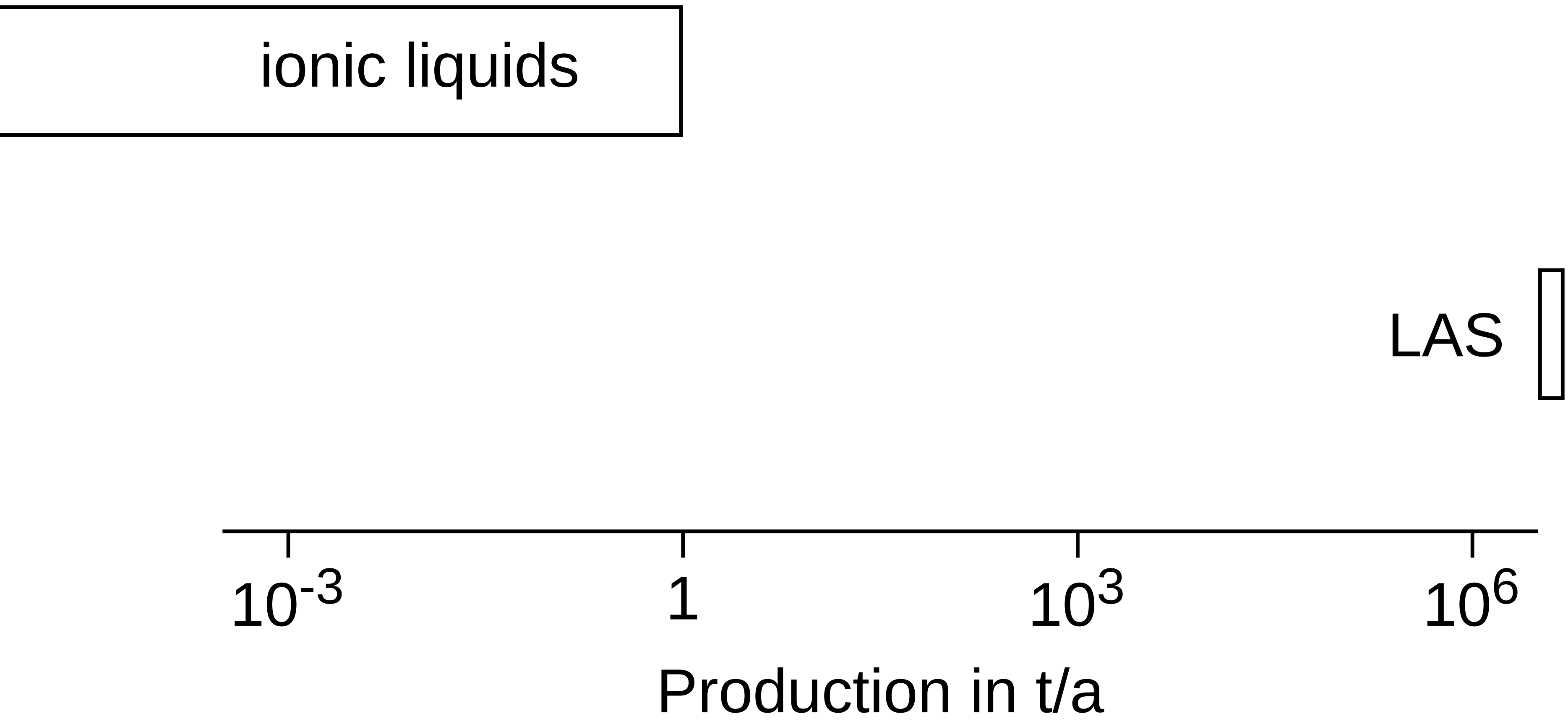
according to Christ, C. *Chem Eng Technol* **1999**, *22*, 642-650

Release



Chemical production process
Residue
Heated water
Product
Waste
Gas
Water
Cooling
Closed cooling system
Utilization
Disposal
Treatment
Treatment
Incineration
Landfill
Leachate
Sewage sludge
Receiving water
Slag, ash

Global production scale



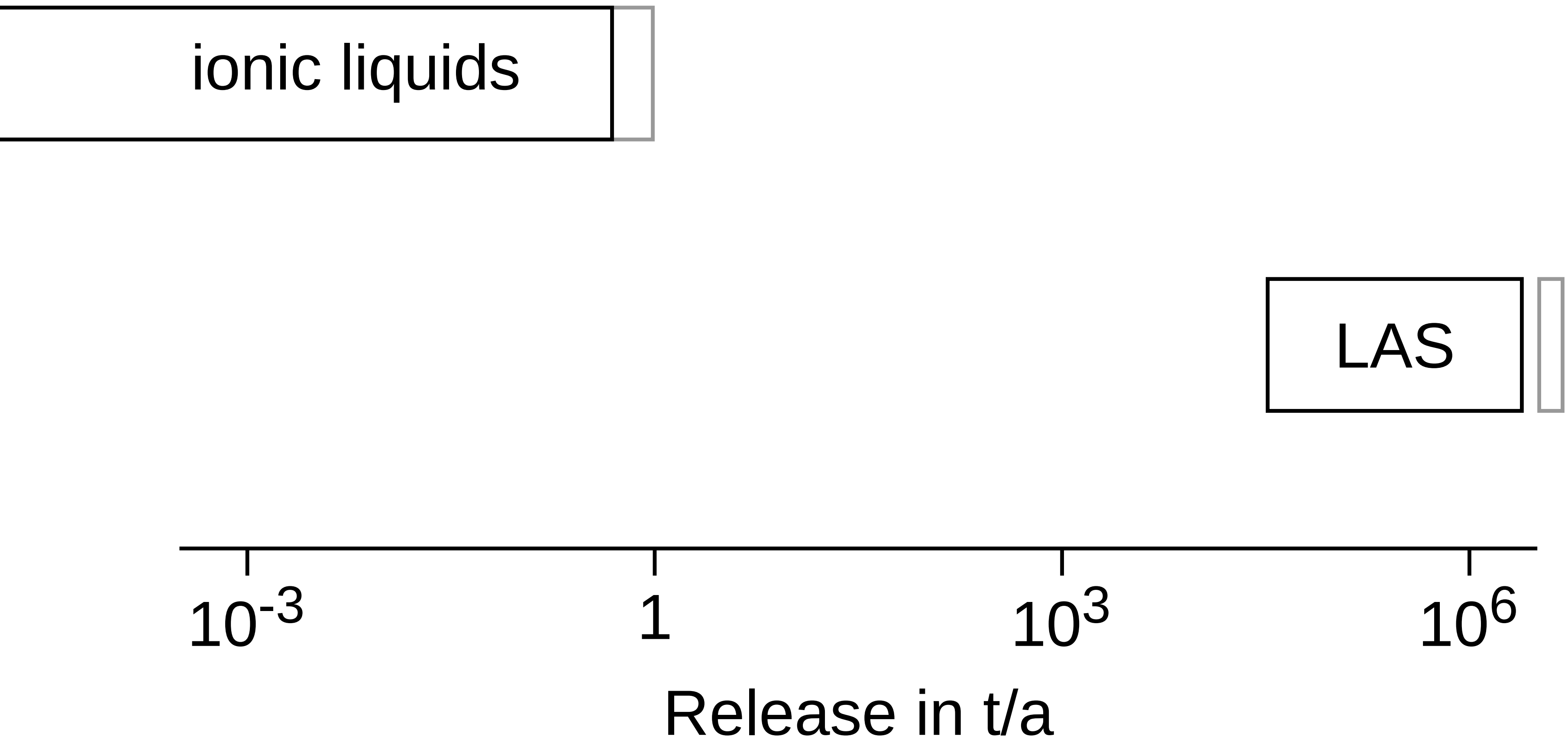
Release factors

- 0.01 to 0.5 for LAS

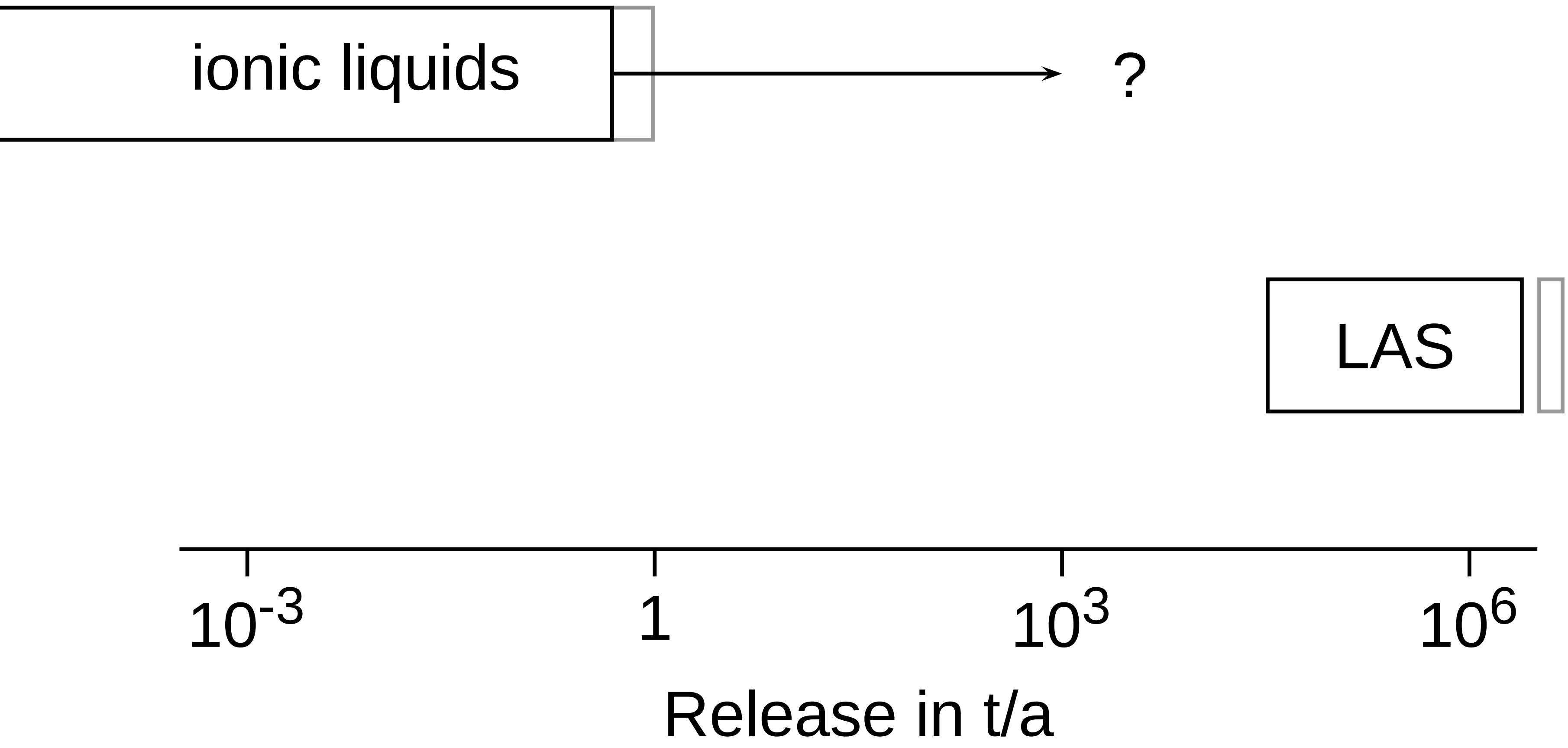
Release factors

- 0.01 to 0.5 for LAS
- 0.001 to 0.5 for IL

Global release scale



Global release scale



Release of ionic liquids

- Impurities can be controlled

Release of ionic liquids

- Impurities can be controlled
- Decomposition can be avoided

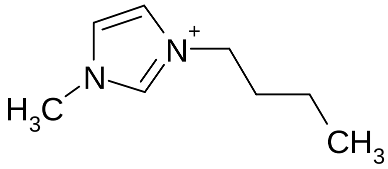
Release of ionic liquids

- Impurities can be controlled
- Decomposition can be avoided
- IL in waste water could be removed

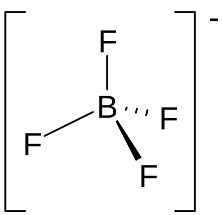
Release of ionic liquids

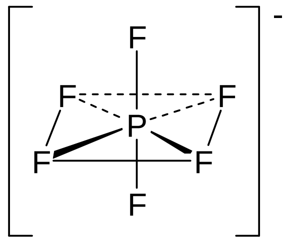
- Impurities can be controlled
- Decomposition can be avoided
- IL in waste water could be removed
- Accidental releases must be considered

Are IL readily biodegradable?

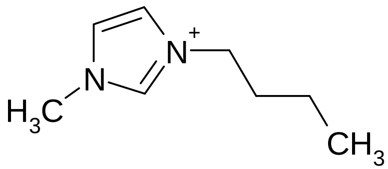


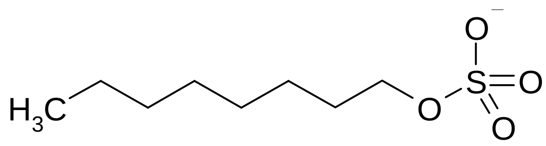
Cl^- Br^-



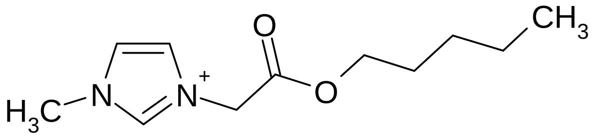


0 - 3 %



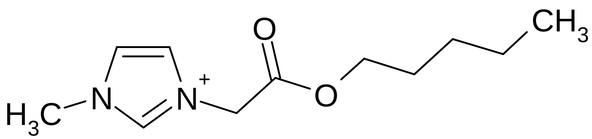


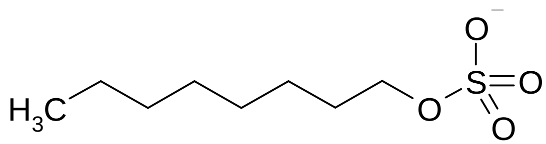
25 %



Br^-

32 / 41 %

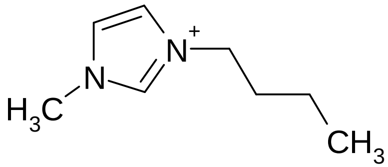




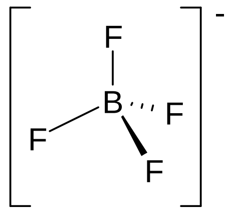
54 / 67 %

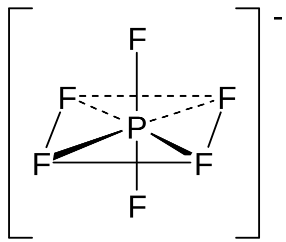
N. Gathergood, M. T. Garcia, and P. J. Scammells. *Green Chem* **2004**, **2005**, **2006**

Are IL readily biodegradable?

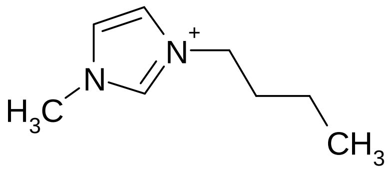


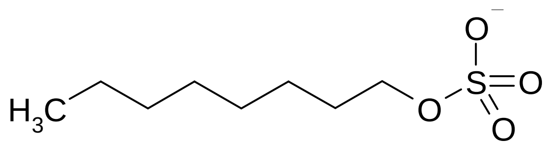
Cl^- Br^-



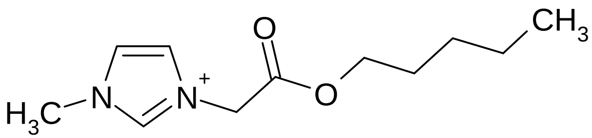


0 - 3 %



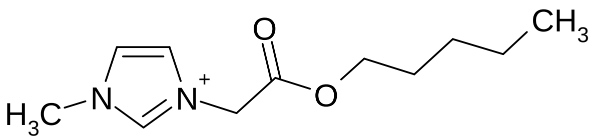


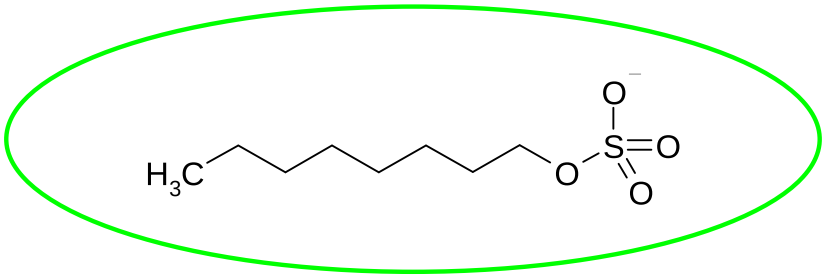
25 %



Br^-

32 / 41 %





54 / 67 %

N. Gathergood, M. T. Garcia, and P. J. Scammells. *Green Chem* **2004**, **2005**, **2006**

Release via wastewater

Fate of cations and anions in STP has to be judged separately!

- Degradation in sewage treatment plants (STP) presumably higher

Release via wastewater

Fate of cations and anions in STP has to be judged separately!

- Degradation in sewage treatment plants (STP) presumably higher
- Sorption of 1-butyl-3-methylimidazolium (bmim) cation presumably low

Release via wastewater

Fate of cations and anions in STP has to be judged separately!

- Degradation in sewage treatment plants (STP) presumably higher
- Sorption of 1-butyl-3-methylimidazolium (bmim) cation presumably low
- Overall removal of bmim presumably incomplete

Release via wastewater

Fate of cations and anions in STP has to be judged separately!

- Degradation in sewage treatment plants (STP) presumably higher
- Sorption of 1-butyl-3-methylimidazolium (bmim) cation presumably low
- Overall removal of bmim presumably incomplete
- Good removal of alkyl sulfates

Spatiotemporal range of IL

Interplay of

- Hydrolysis

Spatiotemporal range of IL

Interplay of

- Hydrolysis
- Biodegradation

Spatiotemporal range of IL

Interplay of

- Hydrolysis
- Biodegradation
- Sorption to organic material and various surfaces

Spatiotemporal range of IL

Interplay of

- Hydrolysis
- Biodegradation
- Sorption to organic material and various surfaces

No fate modelling carried out yet,

$\Rightarrow$ High uncertainty

Bioaccumulation of IL

- Analogy to ionic surfactants

Bioaccumulation of IL

- Analogy to ionic surfactants
- BCF estimation method [1]

[1] Meylan et al. *Environ Toxicol Chem* **1999** *18* 664-672

Bioaccumulation of IL

- Analogy to ionic surfactants
- BCF estimation method [1]
- Some log K_{ow} values [2]

[1] Meylan et al. *Environ Toxicol Chem* **1999** *18* 664-672

[2] Ropel et al. *Green Chem* **2005** *7* 83-90

Bioaccumulation of IL

- Analogy to ionic surfactants
- BCF estimation method [1]
- Some log K_{ow} values [2]
- Partitioning to mammalian cells [3]

[1] Meylan et al. *Environ Toxicol Chem* **1999** *18* 664-672

[2] Ropel et al. *Green Chem* **2005** *7* 83-90

[3] Ranke et al. *Toxicol Env Chem* **2006** *88* 273-285

Bioaccumulation of IL

- Analogy to ionic surfactants
- BCF estimation method [1]
- Some log K_{ow} values [2]
- Partitioning to mammalian cells [3]
- k_0 values from HPLC [4]

[1] Meylan et al. *Environ Toxicol Chem* **1999** *18* 664-672

[2] Ropel et al. *Green Chem* **2005** *7* 83-90

[3] Ranke et al. *Toxicol Env Chem* **2006** *88* 273-285

[4] Ranke et al. *Ecotoxicol Environ Safety* **2006** *in press*

Problems with log K_{ow} for IL

- Experimental difficulties in the case of surface activity

Problems with log K_{ow} for IL

- Experimental difficulties in the case of surface activity
- Dependence on presence of counter-ions

Problems with log K_{ow} for IL

- Experimental difficulties in the case of surface activity
- Dependence on presence of counter-ions
- Shake-flask experiments are time-consuming

log k_0 values from gradient HPLC

- Describe distribution between stationary phase and water (ideally)

log k_0 values from gradient HPLC

- Describe distribution between stationary phase and water (ideally)
- Easily generated by one or more gradient runs

log k_0 values from gradient HPLC

- Describe distribution between stationary phase and water (ideally)
- Easily generated by one or more gradient runs
- Separate lipophilicity assessment of cations and anions

log k_0 values from gradient HPLC

- Describe distribution between stationary phase and water (ideally)
- Easily generated by one or more gradient runs
- Separate lipophilicity assessment of cations and anions
- Good correlation with cytotoxicity

Biological activity of IL (UFT)

Tests on different levels of biological organisation

- Enzymes (AChE, GST, GR)

Biological activity of IL (UFT)

Tests on different levels of biological organisation

- Enzymes (AChE, GST, GR)
- Cells (rat leukemia cell line IPC-81, others)

Biological activity of IL (UFT)

Tests on different levels of biological organisation

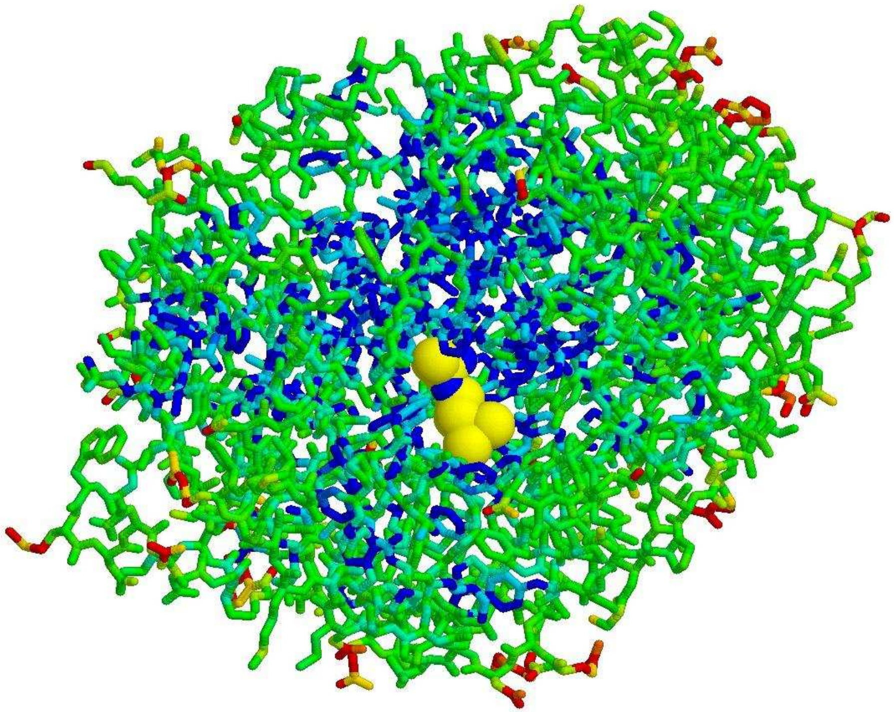
- Enzymes (AChE, GST, GR)
- Cells (rat leukemia cell line IPC-81, others)
- Aquatic organisms (luminescent bacteria, monocellular algae, duckweed)

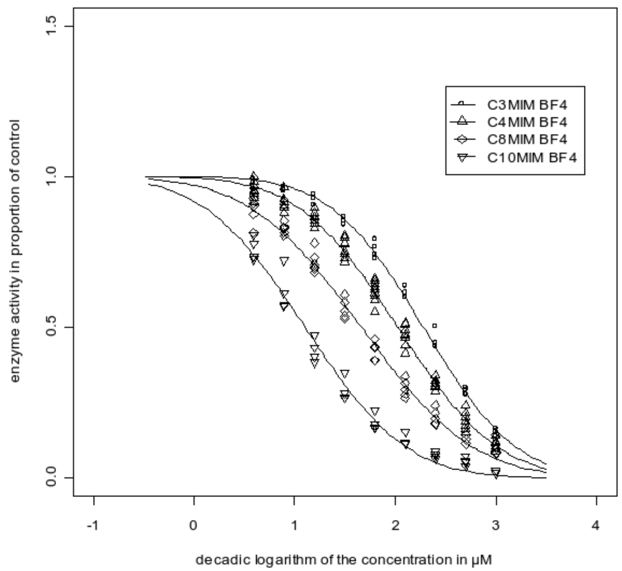
Biological activity of IL (UFT)

Tests on different levels of biological organisation

- Enzymes (AChE, GST, GR)
- Cells (rat leukemia cell line IPC-81, others)
- Aquatic organisms (luminescent bacteria, monocellular algae, duckweed)
- Terrestrial organisms (springtails, enchytraeids, earthworms, terrestrial plants)

Acetylcholinesterase inhibition

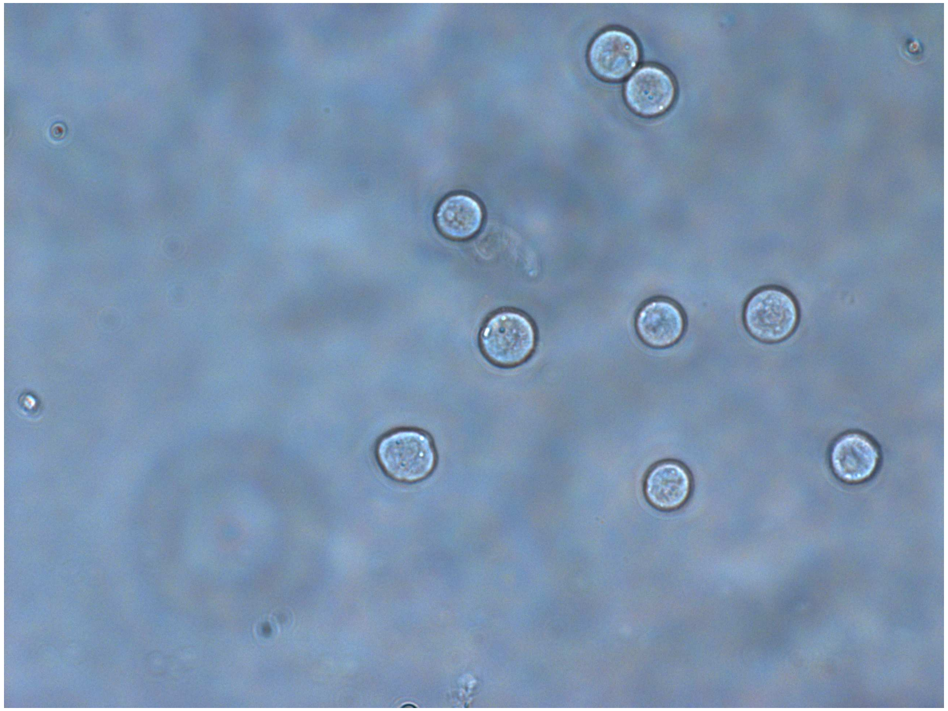


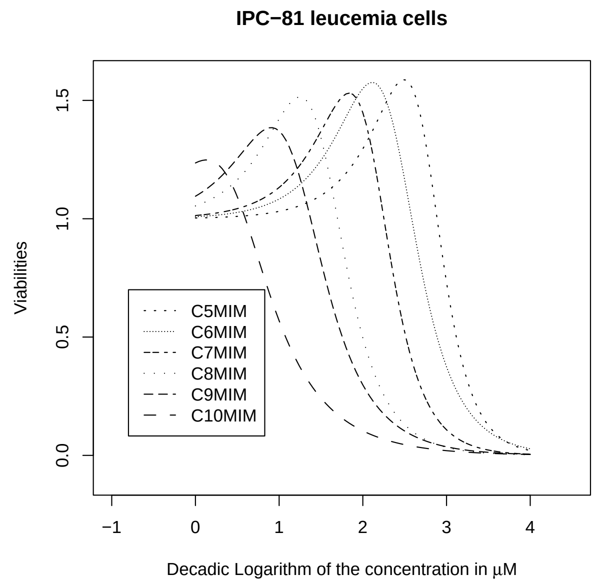


Stock et al. *Green Chem* **2004** *6* 286-290

Arning et al. in preparation

Cell viability assay

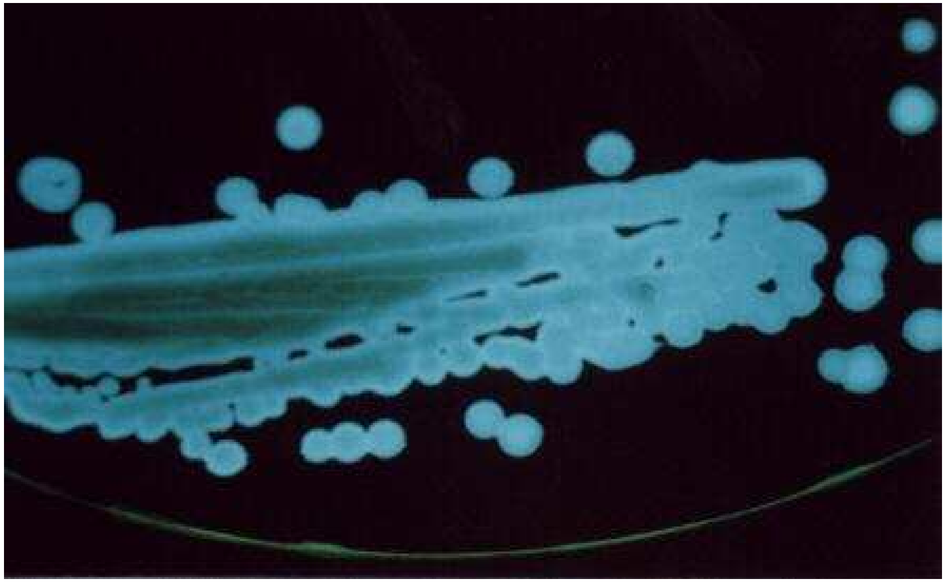


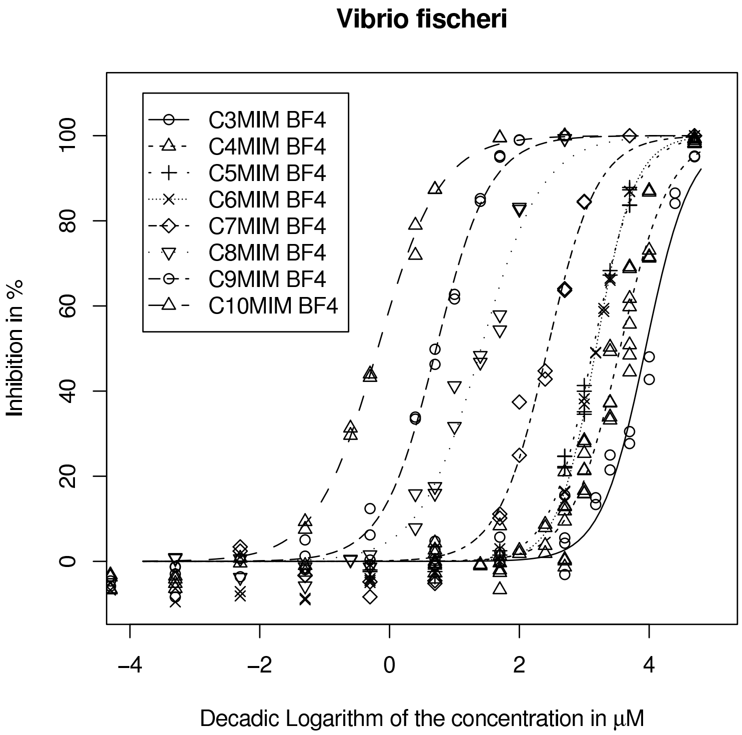


Ranke et al. *Ecotoxicol Environ Safety* **2004** *58* 396-404

Stolte et al. *Green Chem* **2006** *8* 621-629

Luminescence inhibition

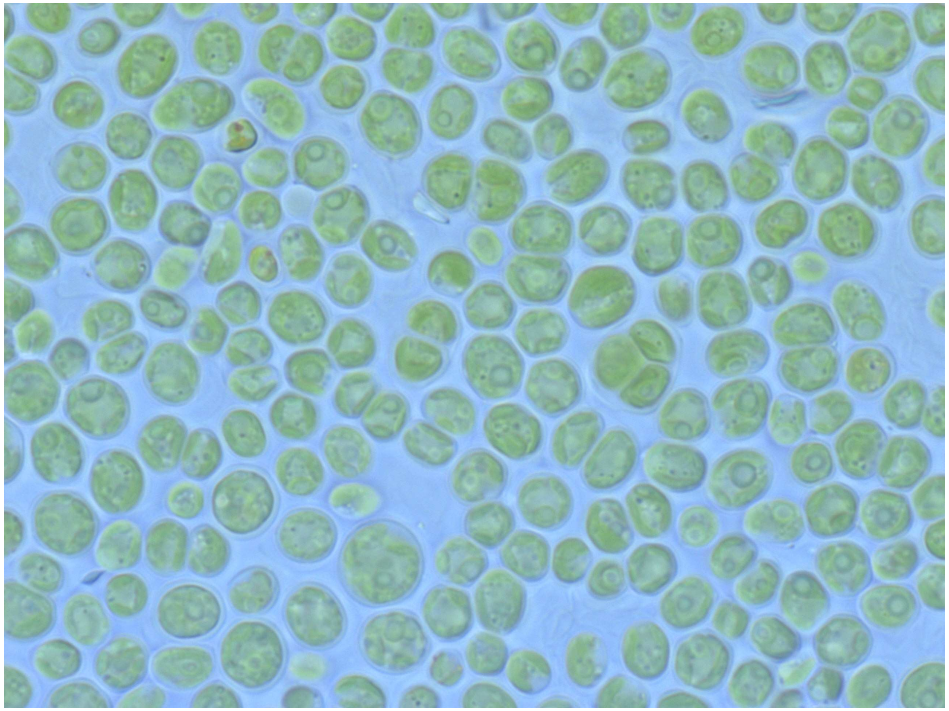




Marine bacteria *Vibrio fischeri*, DIN 38412 L 341

Ranke et al. *Ecotoxicol Environ Safety* **2004** *58* 396-404

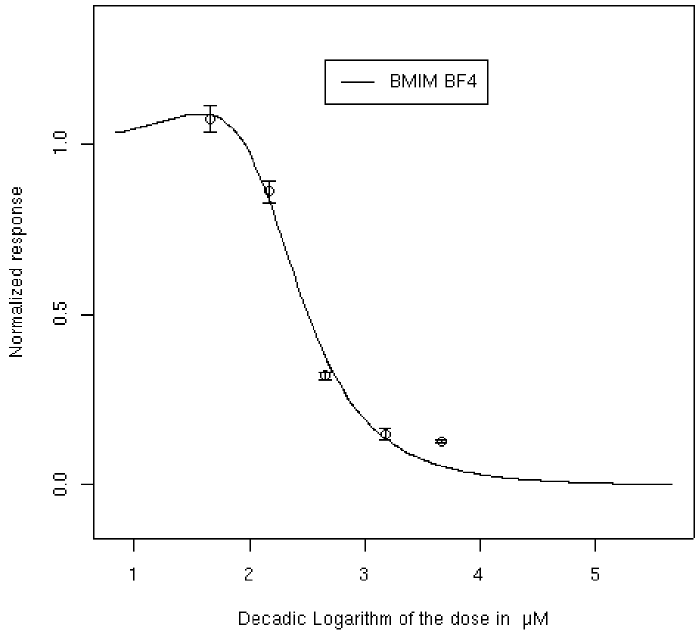
Algae growth inhibition



?

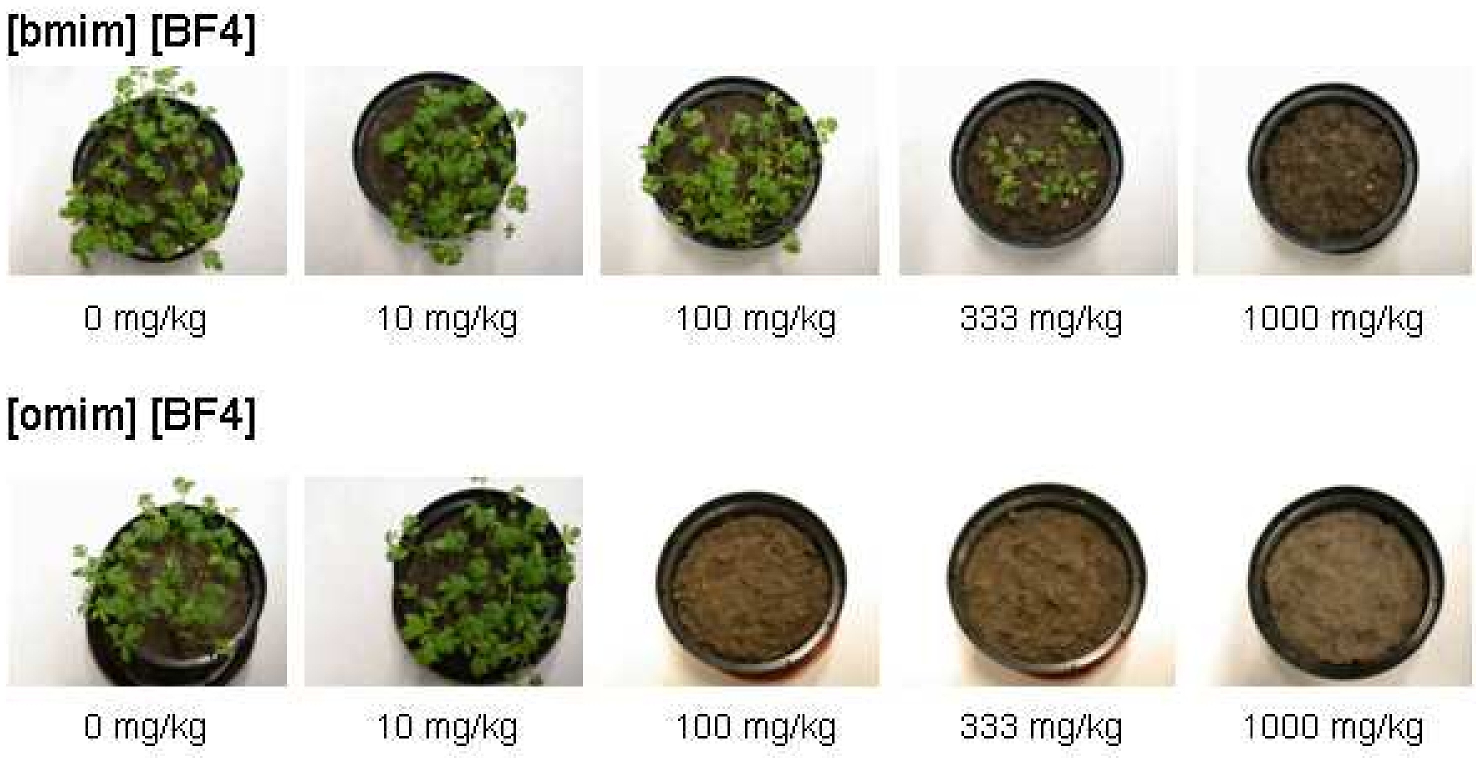
Monocellular algae *Scenedesmus vacuolatus*

Duckweed growth inhibition



Lemna minor, ISO TC 147/SC 5 N draft

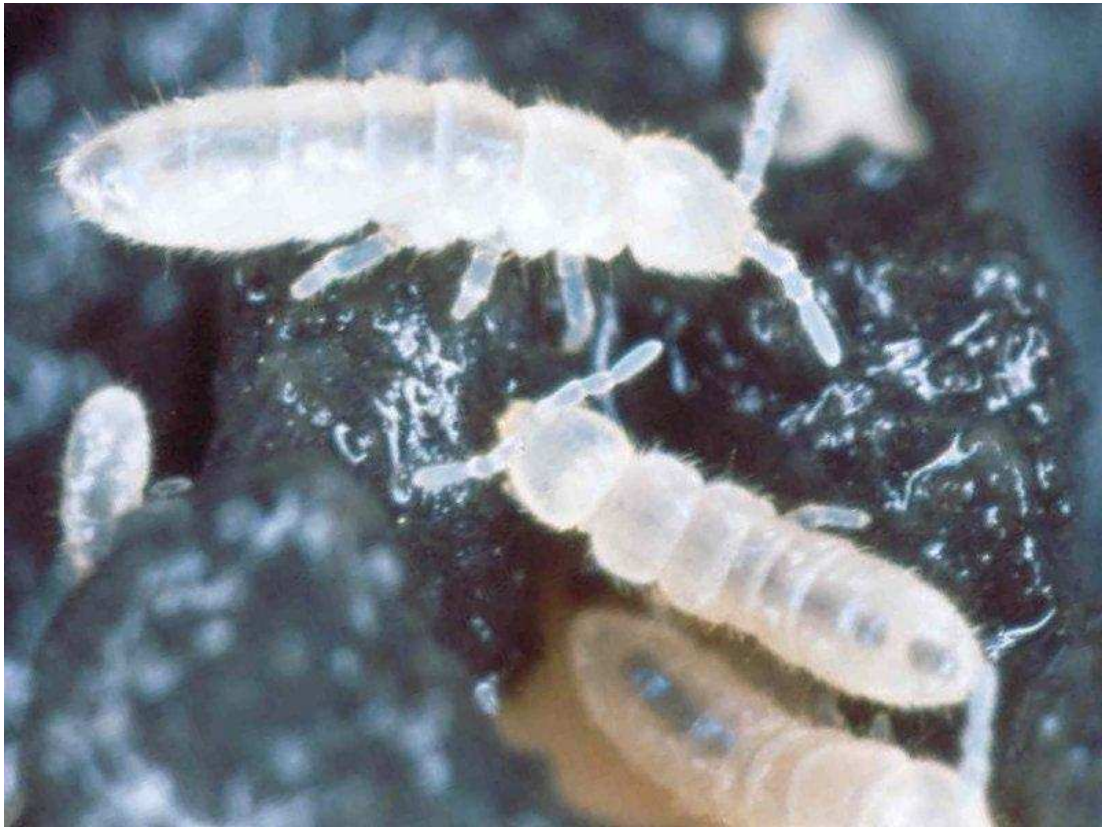
Plant growth inhibition



Lepidium sativum, ISO 11269-2

Jastorff et al. *Green Chem* **2005** *7* 362-372

Inhibition of springtail reproduction



Folsomia candida ISO 11267

Biological activity of IL (literature)

Tests with different organisms

- Aquatic organisms (Luminescent bacteria, monocellular algae, water fleas, zebra fish)

Universität Bremen

UFT

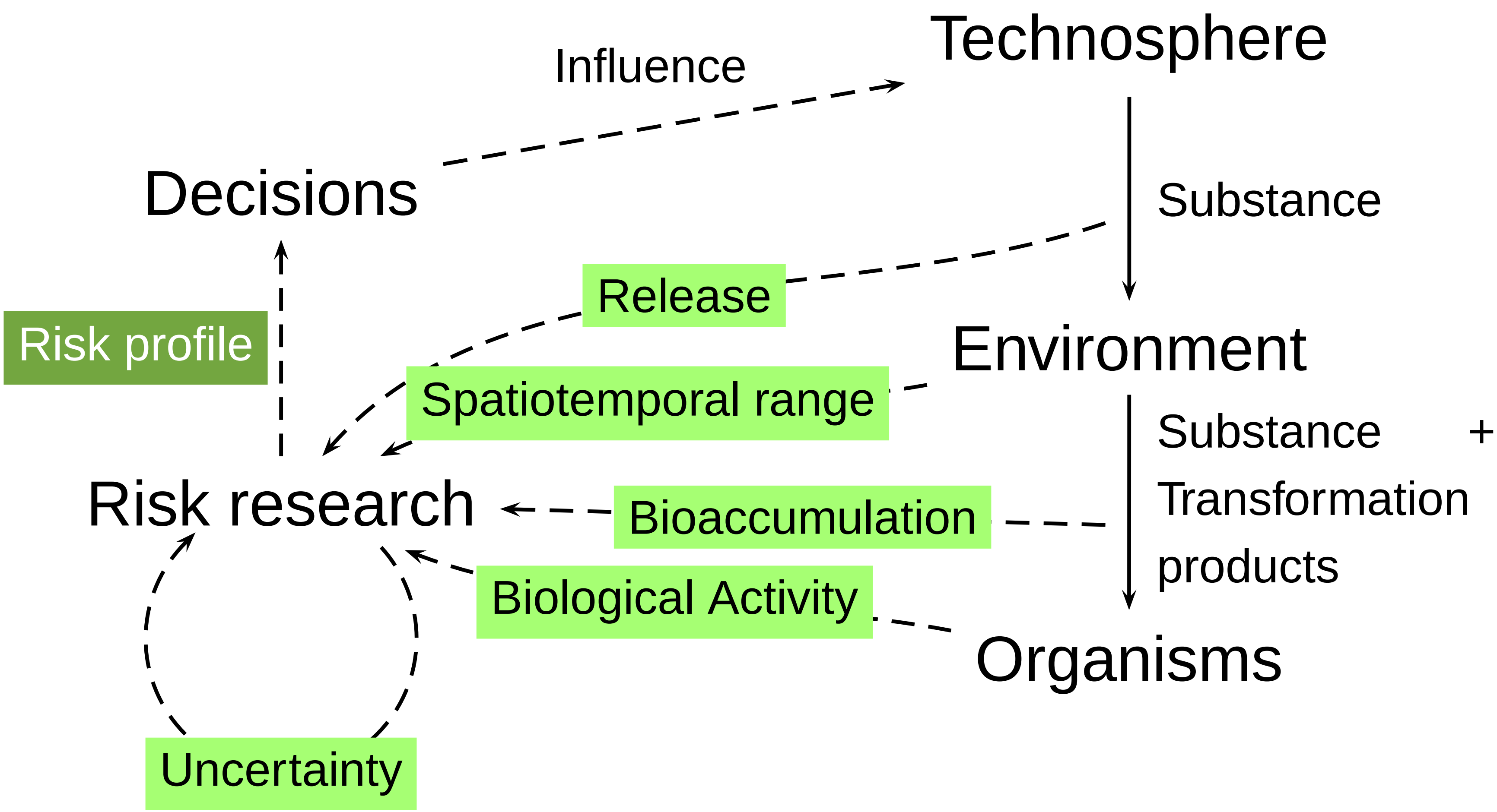
Biological activity of IL (literature)

Tests with different organisms

- Aquatic organisms (Luminescent bacteria, monocellular algae, water fleas, zebra fish)
- Terrestrial organisms (Nematodes, rats, rabbits, mice)

Ranke J (2001) PhD Dissertation

Five risk indicators



Understanding risk related properties

Concepts

- Molecular interaction potentials

Concepts

- Molecular interaction potentials
- Linear free enthalpy relationships (LFER)

Concepts

- Molecular interaction potentials
- Linear free enthalpy relationships (LFER)
- Basal cytotoxicity

Concepts

- Molecular interaction potentials
- Linear free enthalpy relationships (LFER)
- Basal cytotoxicity
- Baseline toxicity

Concepts

- Molecular interaction potentials
- Linear free enthalpy relationships (LFER)
- Basal cytotoxicity
- Baseline toxicity
- Mixture toxicity

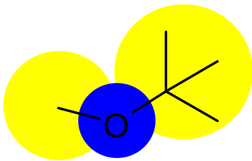
Concepts

- Molecular interaction potentials
- Linear free enthalpy relationships (LFER)
- Basal cytotoxicity
- Baseline toxicity
- Mixture toxicity
- Bioavailability

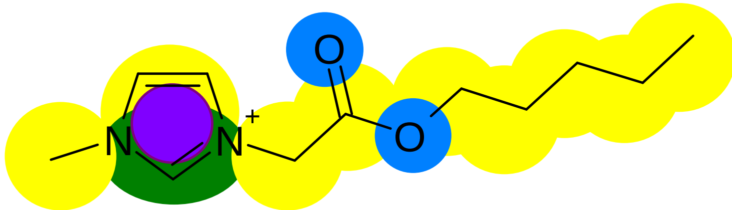
Concepts

- Molecular interaction potentials
- Linear free enthalpy relationships (LFER)
- Basal cytotoxicity
- Baseline toxicity
- Mixture toxicity
- Bioavailability
- Molecular biology

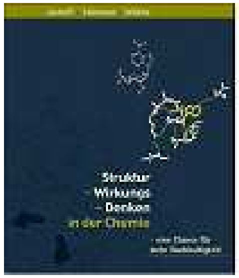
Molecular interaction potentials



MTBE



IM1-1COO5



Jastorff, B., Störmann, R., Wölcke, U.: Strukturr-Wirkungs-Denken in der Chemie — eine Chance für mehr Nachhaltigkeit. Aschenbeck & Isensee, **2003**

Linear Free Energy Relationships

LFERs correlate Gibbs free energies of IL transfer between

- water and pure IL ($\log c_w^{sat}$)

Linear Free Energy Relationships

LFERs correlate Gibbs free energies of IL transfer between

- water and pure IL (log c_w^{sat})
- water and octanol (log K_{ow})

Linear Free Energy Relationships

LFERs correlate Gibbs free energies of IL transfer between

- water and pure IL (log c_w^{sat})
- water and octanol (log K_{ow})
- water and air-water surfaces (surface tension)

Linear Free Energy Relationships

LFERs correlate Gibbs free energies of IL transfer between

- water and pure IL (log c_w^{sat})
- water and octanol (log K_{ow})
- water and air-water surfaces (surface tension)
- water and C18-silica (log k_0)

Linear Free Energy Relationships

LFERs correlate Gibbs free energies of IL transfer between

- water and pure IL (log c_w^{sat})
- water and octanol (log K_{ow})
- water and air-water surfaces (surface tension)
- water and C18-silica (log k_0)
- water and artificial membranes or biota

Linear Free Energy Relationships

LFERs correlate Gibbs free energies of IL transfer between

- water and pure IL (log c_w^{sat})
- water and octanol (log K_{ow})
- water and air-water surfaces (surface tension)
- water and C18-silica (log k_0)
- water and artificial membranes or biota
- water and cytotoxicity target sites (log EC_{50})

Linear Free Energy Relationships

LFERs correlate Gibbs free energies of IL transfer between

- water and pure IL (log c_w^{sat})
- water and octanol (log K_{ow})
- water and air-water surfaces (surface tension)
- $\boxed{\text{water and C18-silica (log } k_0\text{)}}$
- water and artificial membranes or biota
- $\boxed{\text{water and cytotoxicity target sites (log } EC_{50}\text{)}}$

The hypothesis of a basal cytotoxicity

- toxicity to basal functions of all cells of an organism

Ekwall *Acta Pharmacol Toxicol* **1983** *95 Suppl 2* 80-99

The hypothesis of a basal cytotoxicity

- toxicity to basal functions of all cells of an organism
- as opposed to organ specific or extracellular toxicity

Ekwall *Acta Pharmacol Toxicol* **1983** *95 Suppl 2* 80-99

The hypothesis of a basal cytotoxicity

- toxicity to basal functions of all cells of an organism
- as opposed to organ specific or extracellular toxicity
- similar across many in-vitro cytotoxicity tests

Ekwall *Acta Pharmacol Toxicol* **1983** *95 Suppl 2* 80-99

Universität Bremen

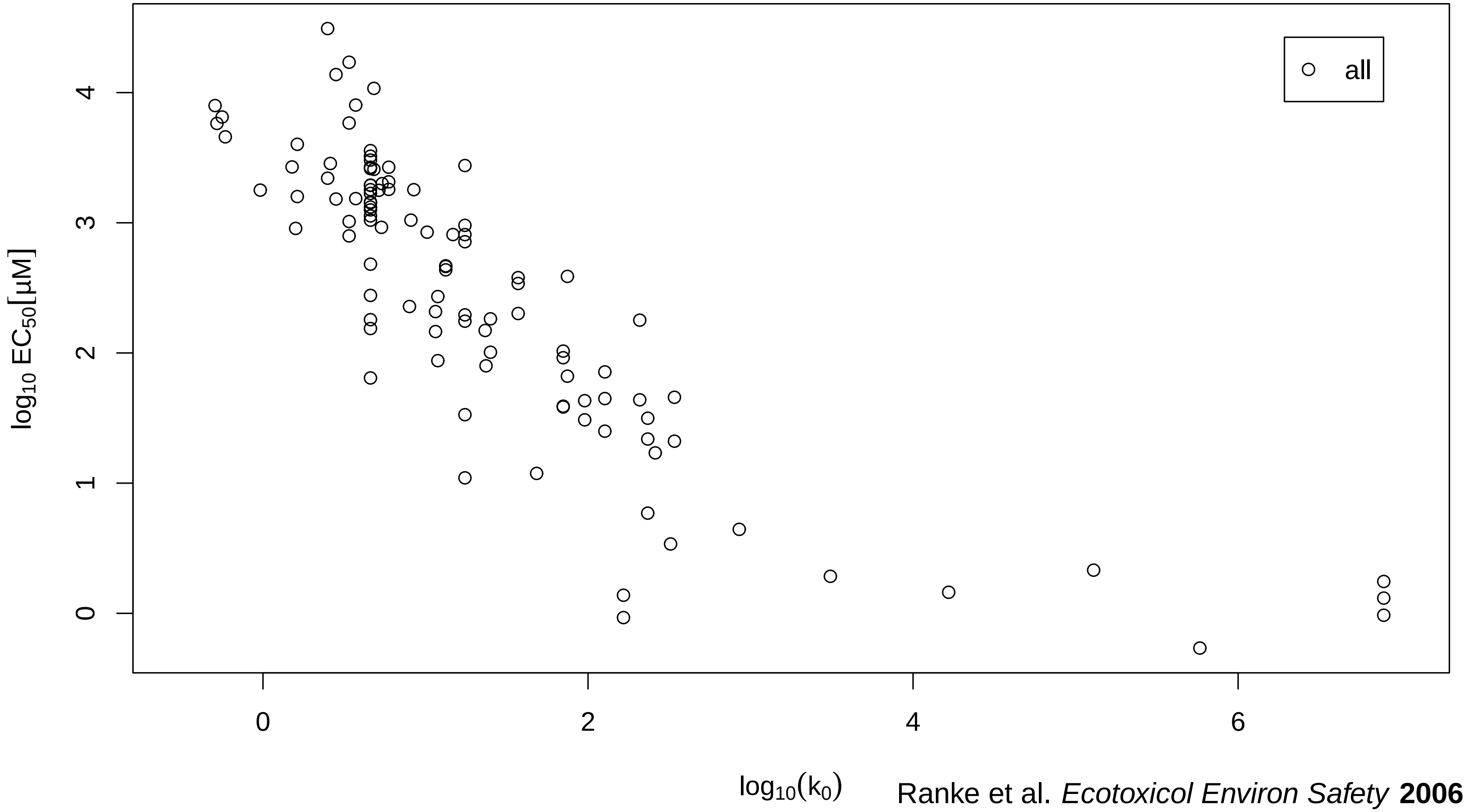
UFT

The hypothesis of a basal cytotoxicity

- toxicity to basal functions of all cells of an organism
- as opposed to organ specific or extracellular toxicity
- similar across many in-vitro cytotoxicity tests
- similar across very different organisms

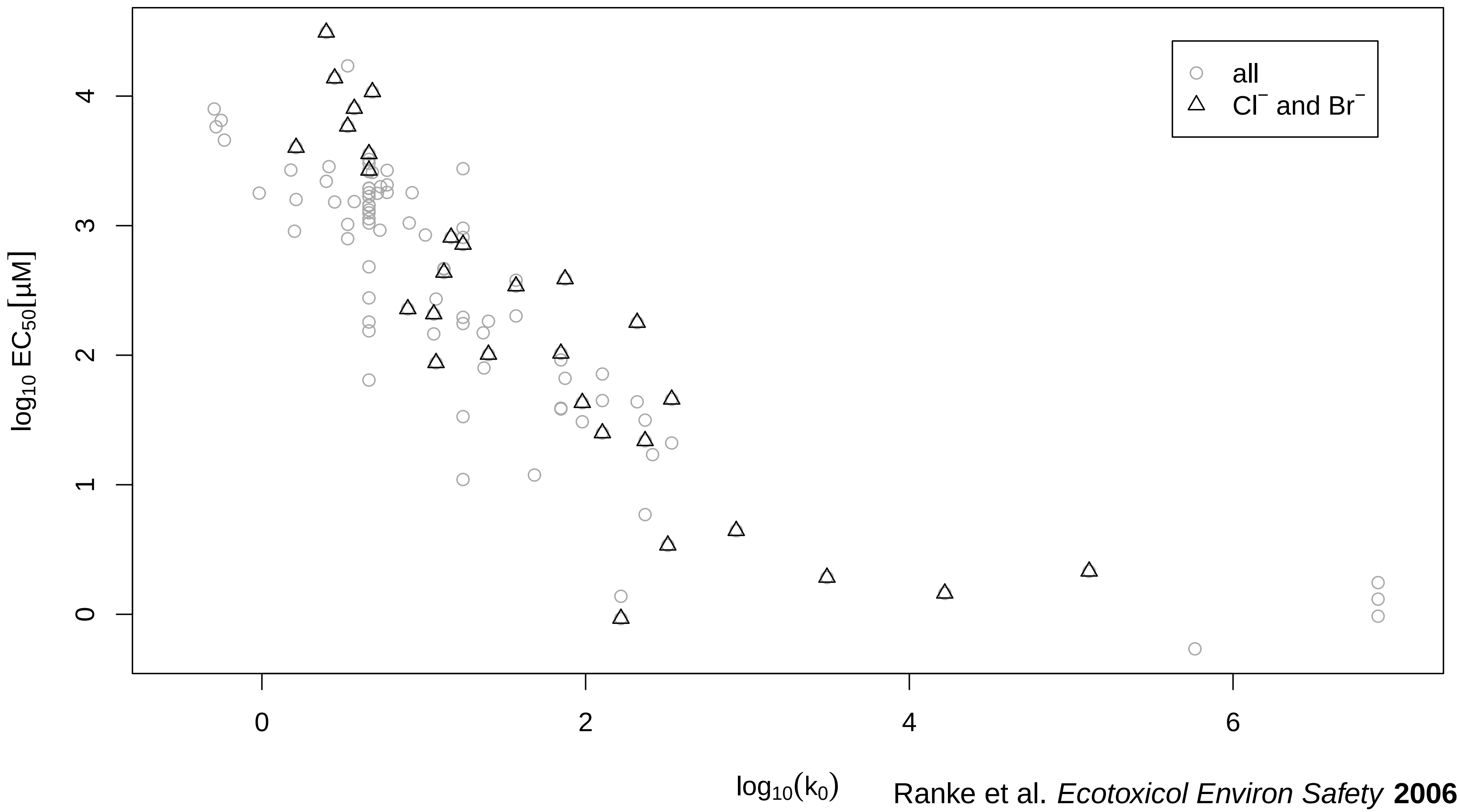
Ekwall *Acta Pharmacol Toxicol* **1983** *95 Suppl 2* 80-99

Cation lipophilicity and cytotoxicity



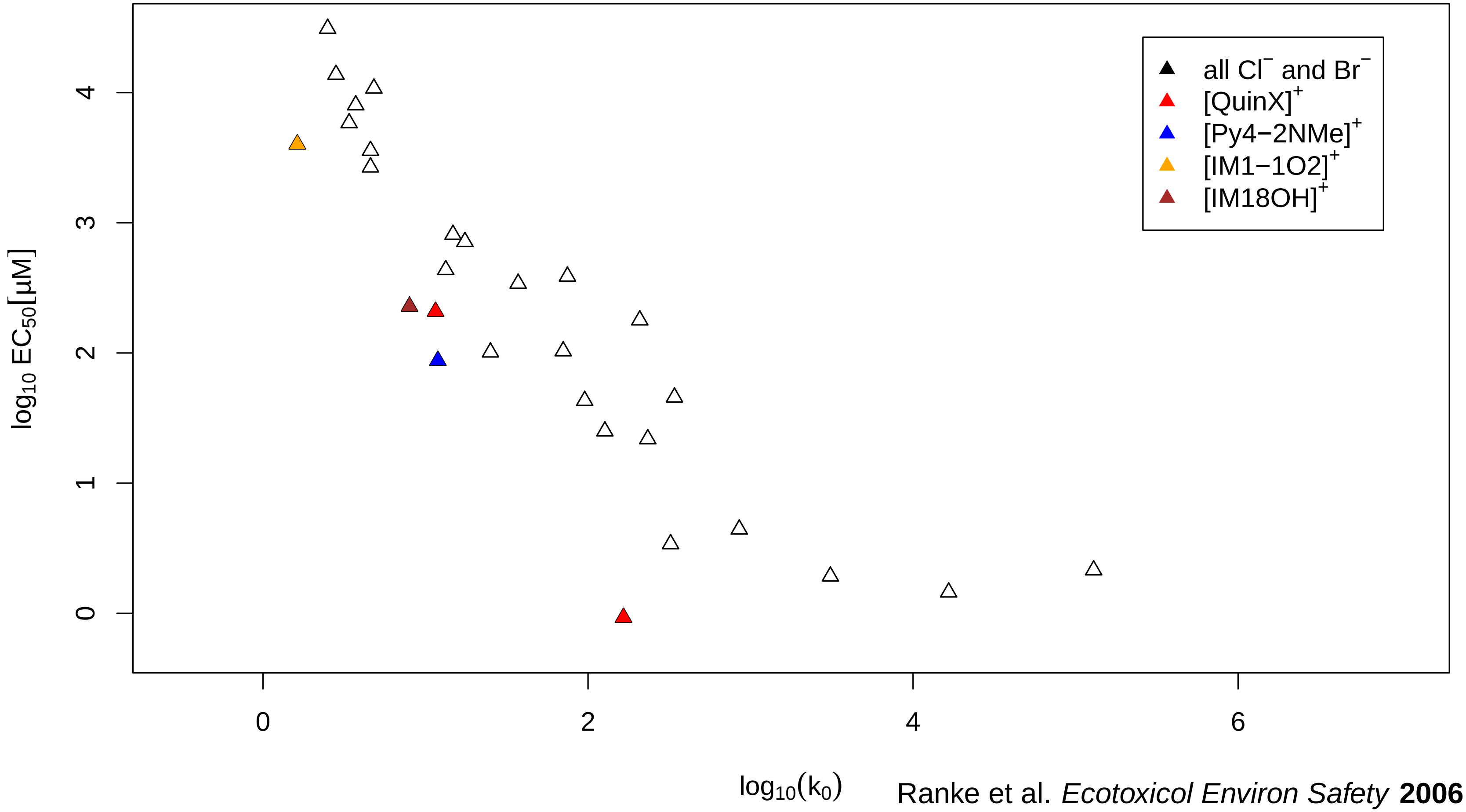
Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



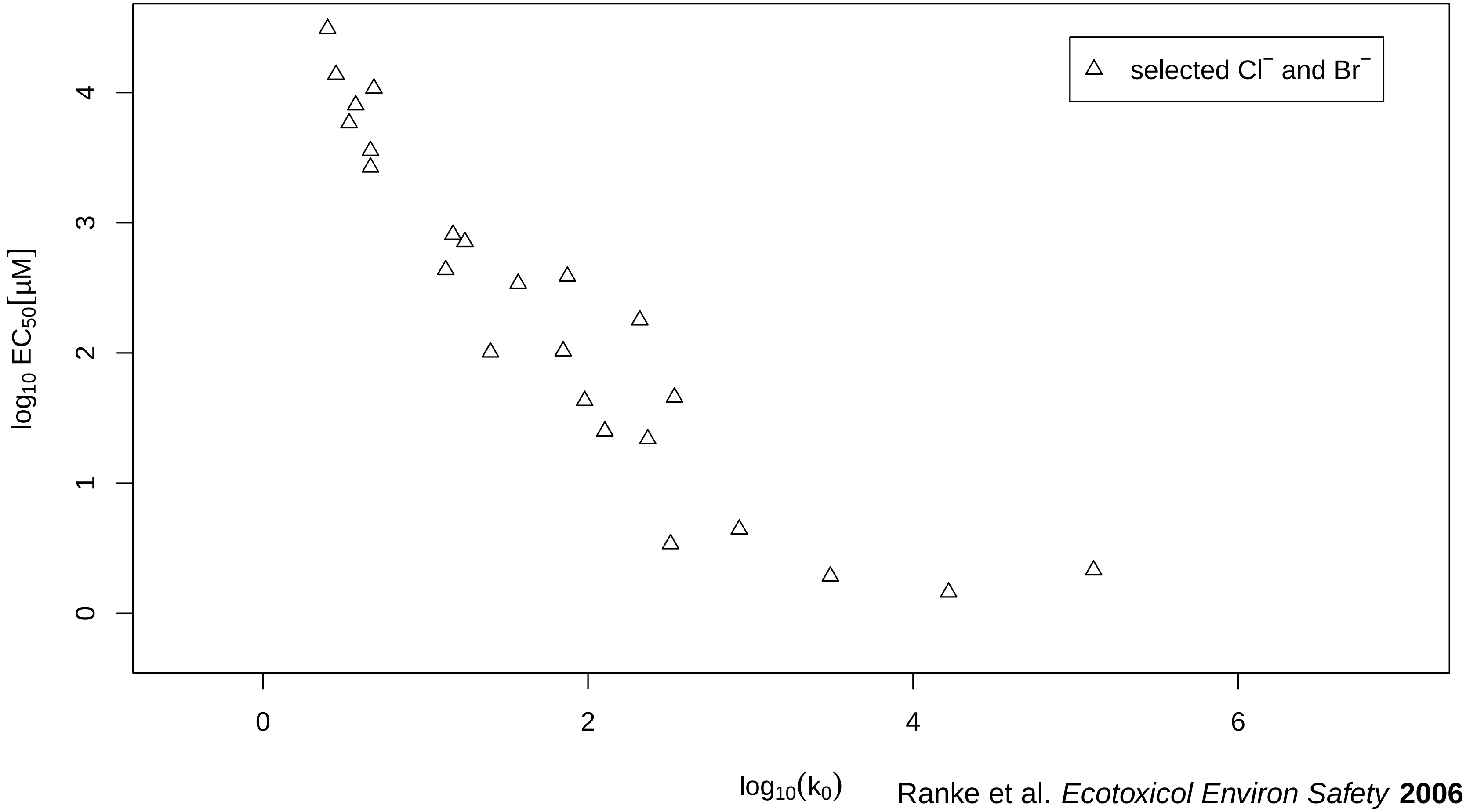
Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



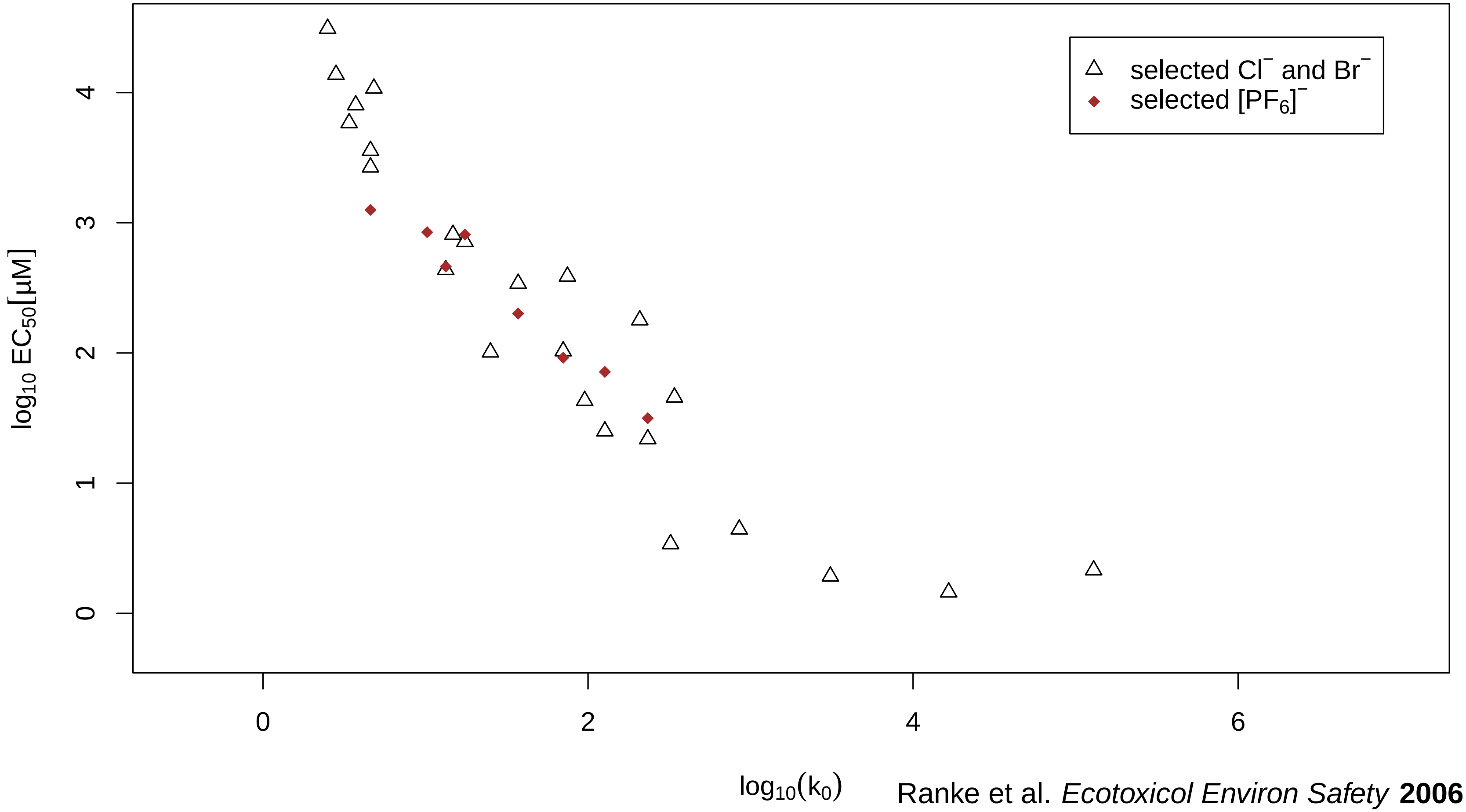
Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



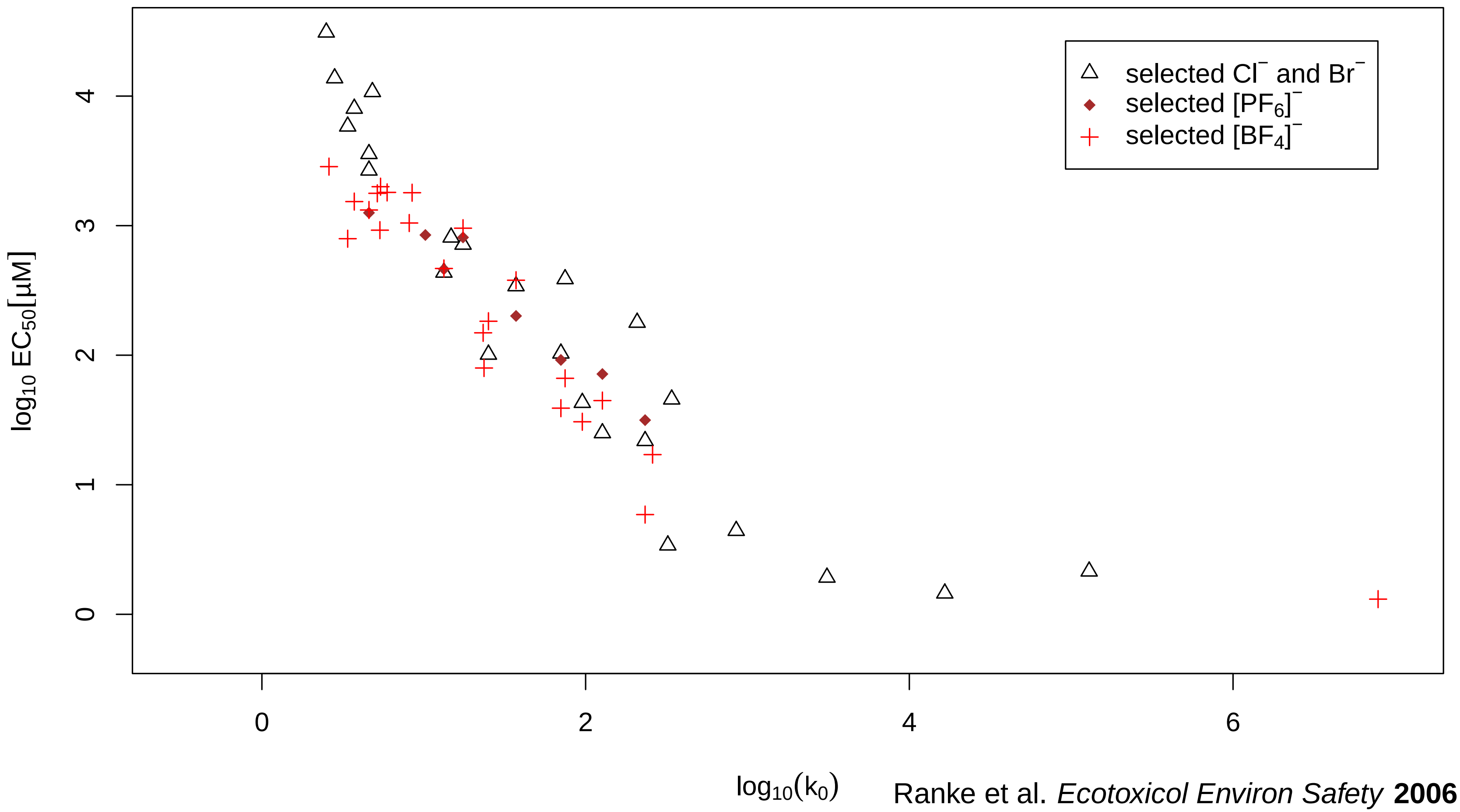
Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



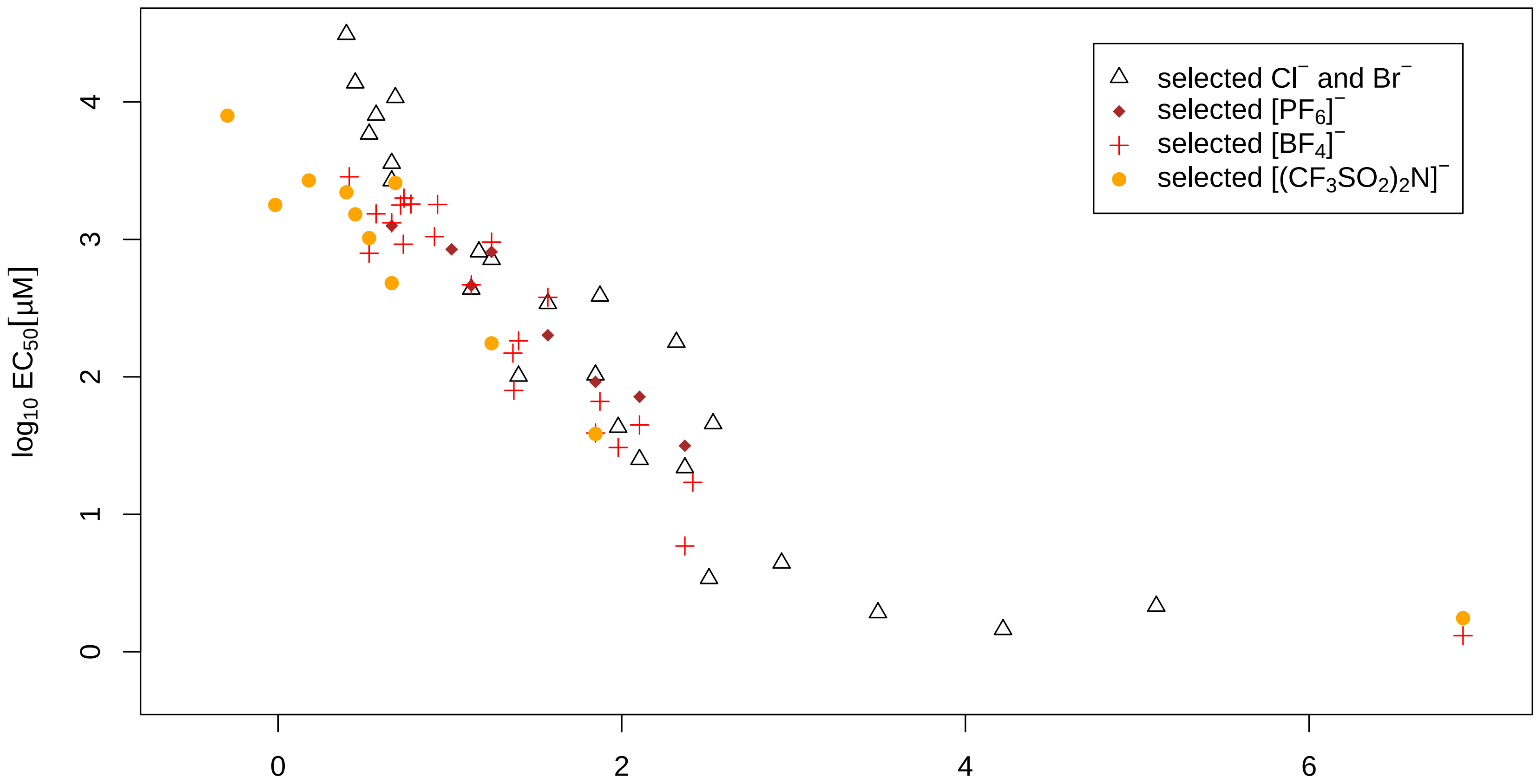
Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Mixture toxicity

Binary 1:1 mixtures of cations and anions

Mixture toxicity

Binary 1:1 mixtures of cations and anions

If concentration addition is assumed:

$$\mathrm{EC}_{50}^{1+2} = \frac{\mathrm{EC}_{50}^{1} \cdot \mathrm{EC}_{50}^{2}}{\mathrm{EC}_{50}^{1} + \mathrm{EC}_{50}^{2}}$$

Mixture toxicity

Binary 1:1 mixtures of cations and anions

If concentration addition is assumed:

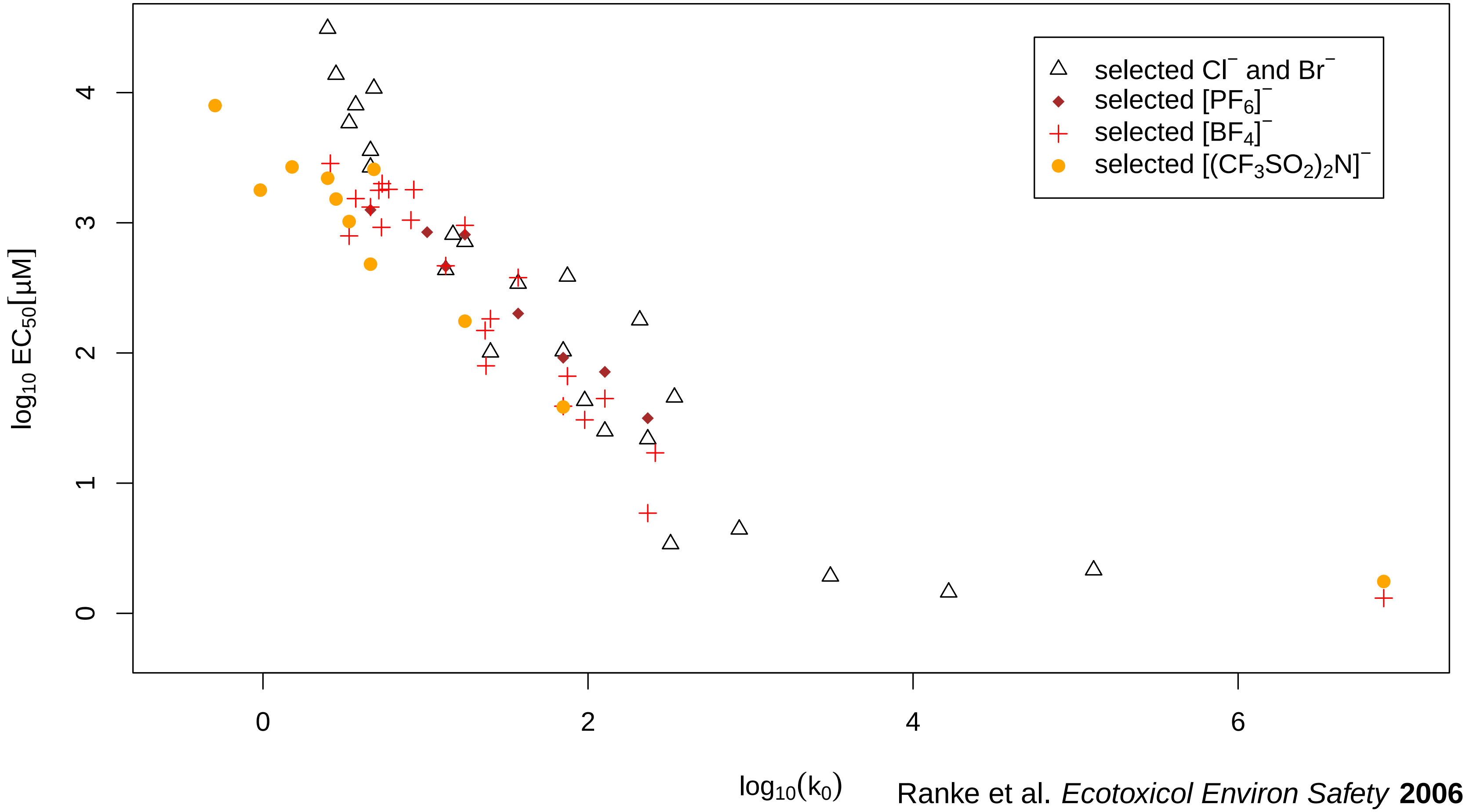
$$\mathrm{EC}_{50}^{1+2} = \frac{\mathrm{EC}_{50}^{1} \cdot \mathrm{EC}_{50}^{2}}{\mathrm{EC}_{50}^{1} + \mathrm{EC}_{50}^{2}}$$

Examples:

$\mathrm{EC}_{50}^{1} = \mathrm{EC}_{50}^{2} = 10\mu\mathrm{M}$: $\quad \mathrm{EC}_{50}^{1+2} = 5\mu\mathrm{M}$

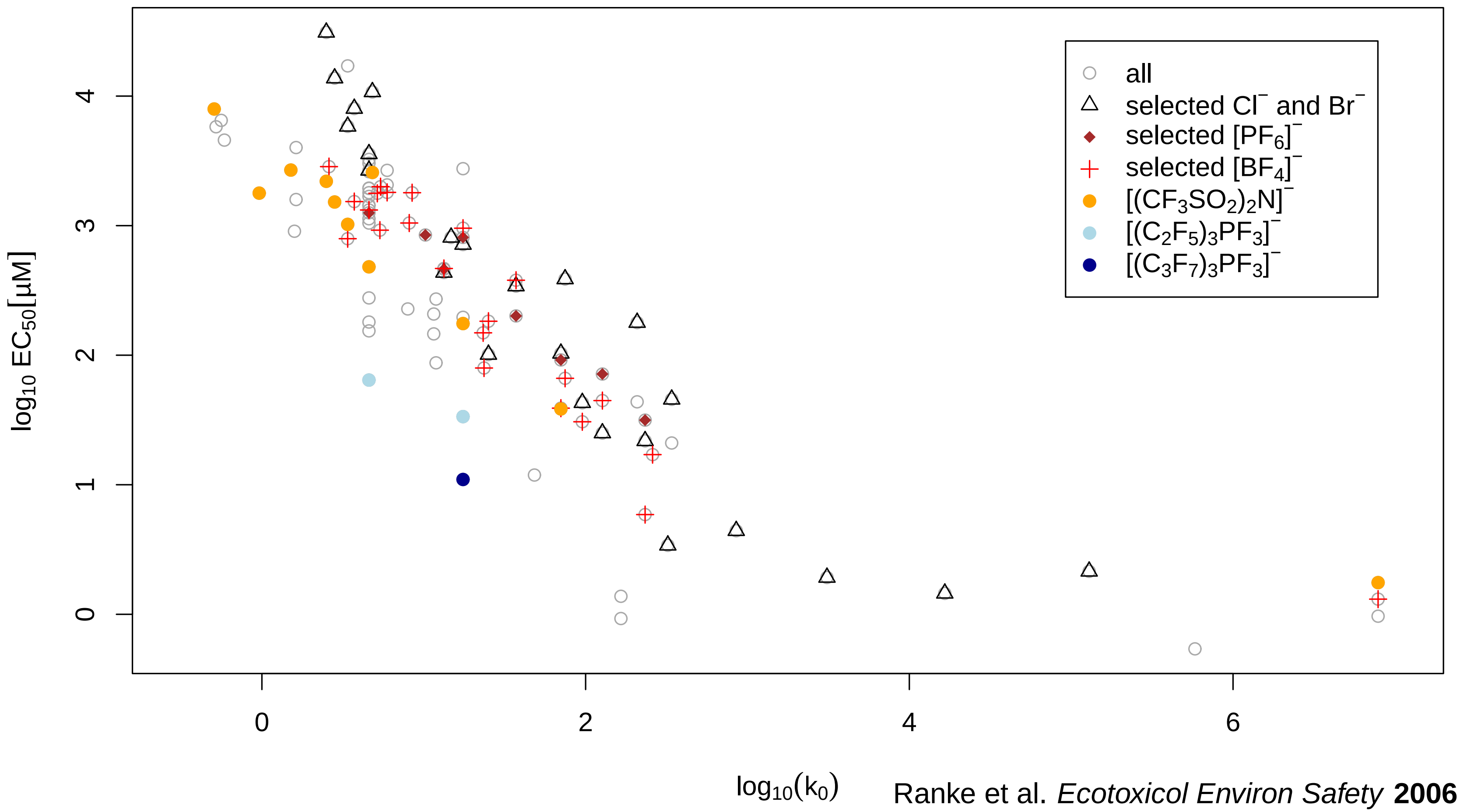
$\mathrm{EC}_{50}^{1} = 100\mu\mathrm{M}$ and $\mathrm{EC}_{50}^{2} = 1\mu\mathrm{M}$: $\quad \mathrm{EC}_{50}^{1+2} = 0.99\mu\mathrm{M}$

Cation lipophilicity and cytotoxicity



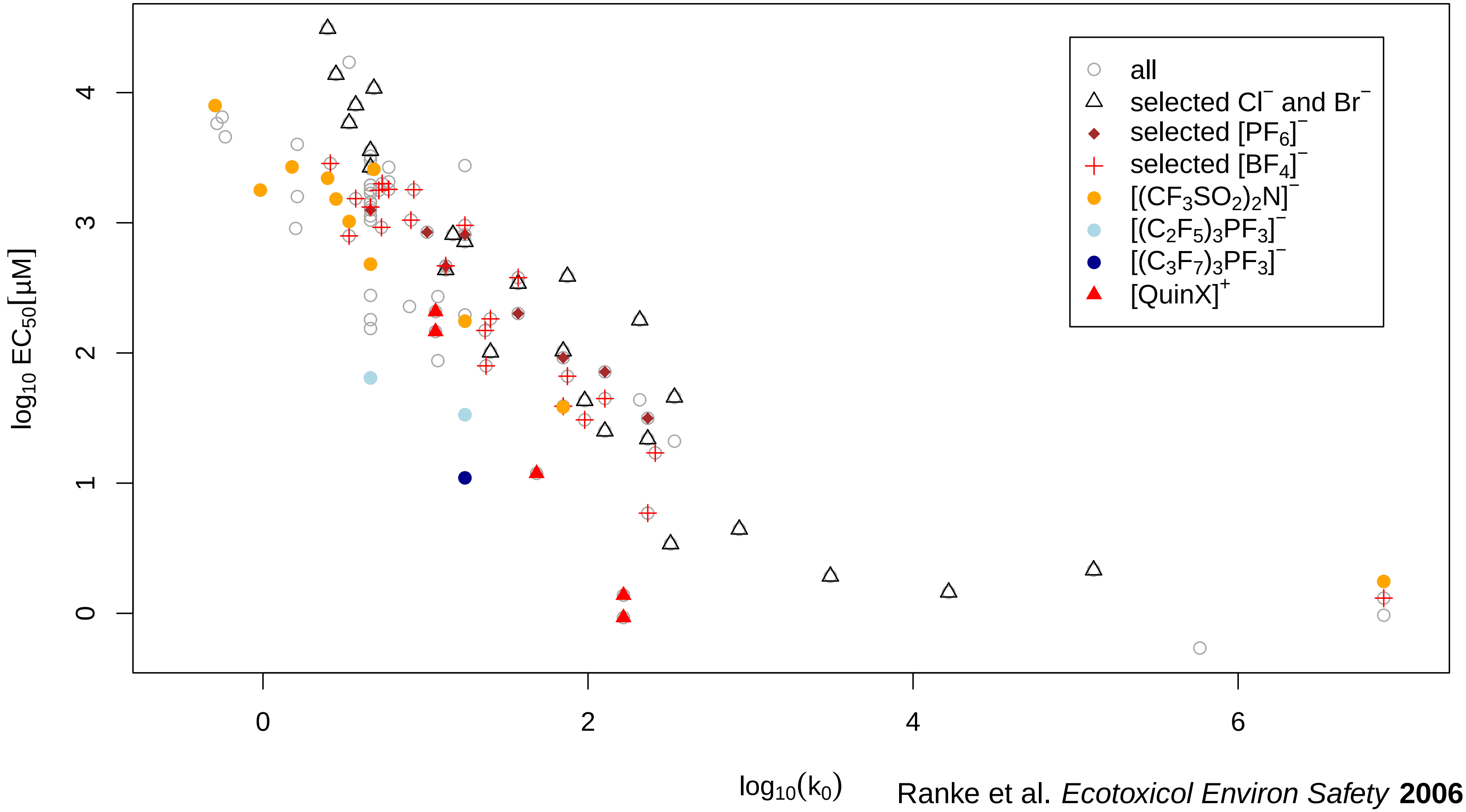
Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

Cation lipophilicity and cytotoxicity



Ranke et al. *Ecotoxicol Environ Safety* **2006** in press
Stolte et al., in preparation

IL baseline cytotoxicity

Exceptions to the rule:

- quinolinium or dimethylaminopyridinium headgroup

IL baseline cytotoxicity

Exceptions to the rule:

- quinolinium or dimethylaminopyridinium headgroup
- hydrophobic or reactive anions

Conclusions

Conclusions I

Many IL are not inherently green

- there is a possibility of thermal decomposition to unknown products

Conclusions I

Many IL are not inherently green

- there is a possibility of thermal decomposition to unknown products
- most of the ions used are not readily biodegradable

Conclusions I

Many IL are not inherently green

- there is a possibility of thermal decomposition to unknown products
- most of the ions used are not readily biodegradable
- some of the ions have a high basal cytotoxicity

Conclusions I

Many IL are not inherently green

- there is a possibility of thermal decomposition to unknown products
- most of the ions used are not readily biodegradable
- some of the ions have a high basal cytotoxicity
- some IL have a high aquatic toxicity

Conclusions II

But there are good news!

- knowledge about long term thermal stability is building up

Universität Bremen

UFT

Conclusions II

But there are good news!

- knowledge about long term thermal stability is building up
- IL are being optimized for biodegradability

Conclusions II

But there are good news!

- knowledge about long term thermal stability is building up
- IL are being optimized for biodegradability
- many of the ions have a low basal cytotoxicity

Conclusions II

But there are good news!

- knowledge about long term thermal stability is building up
- IL are being optimized for biodegradability
- many of the ions have a low basal cytotoxicity
- some IL have low aquatic and terrestrial toxicity

Acknowledgments

- Coauthors

Acknowledgments

- Coauthors
- **Merck KGaA, Darmstadt**

Acknowledgments

- Coauthors
- **Merck KGaA, Darmstadt**
- FSU Jena

Acknowledgments

- Coauthors
- **Merck KGaA, Darmstadt**
- FSU Jena
- IOLITEC, Solvent innovation and other cooperation partners

Acknowledgments

- Coauthors
- **Merck KGaA, Darmstadt**
- FSU Jena
- IOLITEC, Solvent innovation and other cooperation partners
- Prof. R. Schwarzenbach and
  Prof. K. Hungerbühler, ETH Zürich

www.uft.uni-bremen.de

Acknowledgments

- Coauthors
- **Merck KGaA, Darmstadt**
- FSU Jena
- IOLITEC, Solvent innovation and other cooperation partners
- Prof. R. Schwarzenbach and Prof. K. Hungerbühler, ETH Zürich
- Prof. B. Jastorff, Universität Bremen

www.uft.uni-bremen.de