Současná ekotoxikologie
úvod

Luděk Bláha
RECETOX, Přírodovědecká fakulta, Masarykova Universita, Brno

FSS MU Brno, 23.9.2008

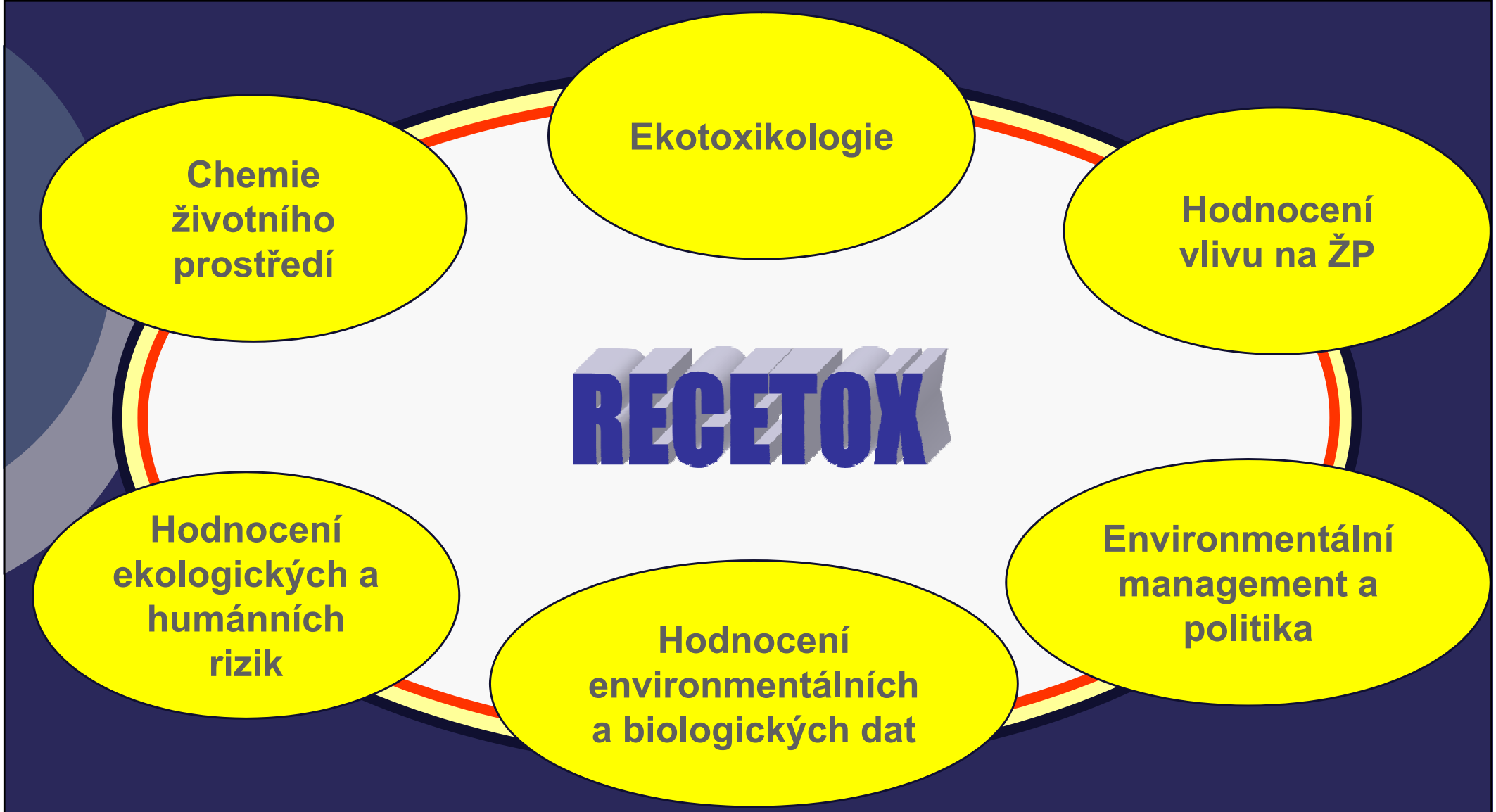
www.**RECETOX**.cz

= Výzkumné centrum pro chemii životního prostředí a ekotoxikologii

EU-DG Research Centre of Excellence for Environmental Chemistry and Ecotoxicology

RECETOX


RECETOX
60



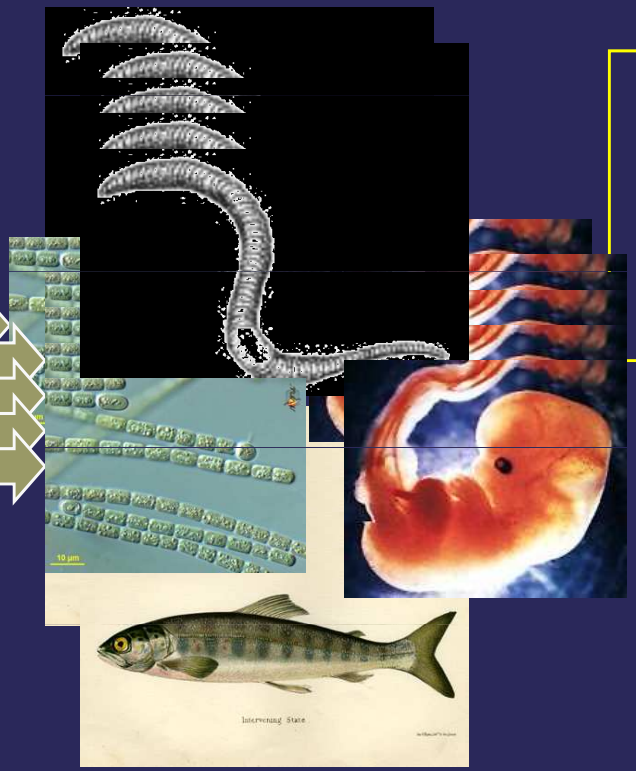
- Výzkum - analytika a procesy v ŽP, ekotoxikologie
- VŠ Výuka - Bc, Mgr, DSP (Chemie - CHŽP, Biologie - Ekotoxikologie, Matematická biologie)
- Env. praxe - projekty - MONET, MVKS, Hodnocení rizik …
- Env. politika - POPs

Chemické znečištění životního prostředí a ekosystémů

Chemikálie v
CHEMICAL
ENVIRONMENT

Hladiny, osud,
LEVELS, FATE,
PROCESSES

Biodostupnost
Bioavailable
fraction



"Expozice"

akutní

chronická

Chemikálie v
CHEMICAL
ENVIRONMENT

biomonitoring

ORGANISM

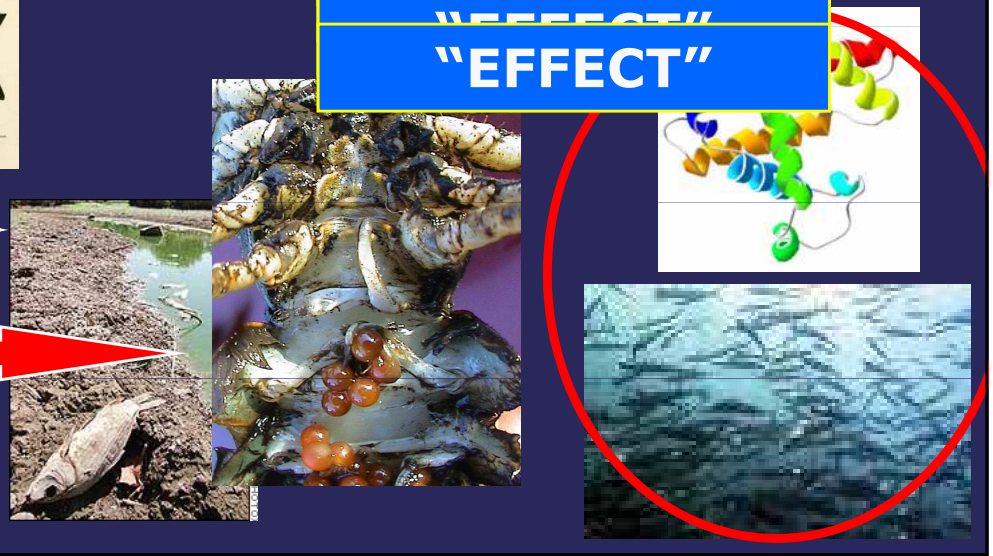
Toxikokinetika
Toxikokinetics

bioaktivace, biotransformace, bioakumulace

excretion, elimination

target site

"EFFECT"



EKOTOXIKOLOGIE

- Věda studující toxické efekty v přírodě, u přírodních organismů, zejména efekty v populacích a společenstvech
(nehumánní toxikologie)
Truhaut 1979

Věda studující efekty chemického (i ostatního stresu) v ekosystémech, **včetně efektů na člověka**

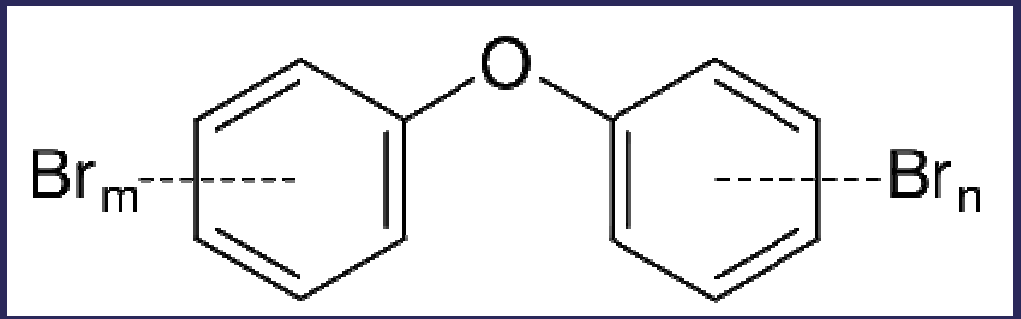
Hlavní cíle ekotoxikologie

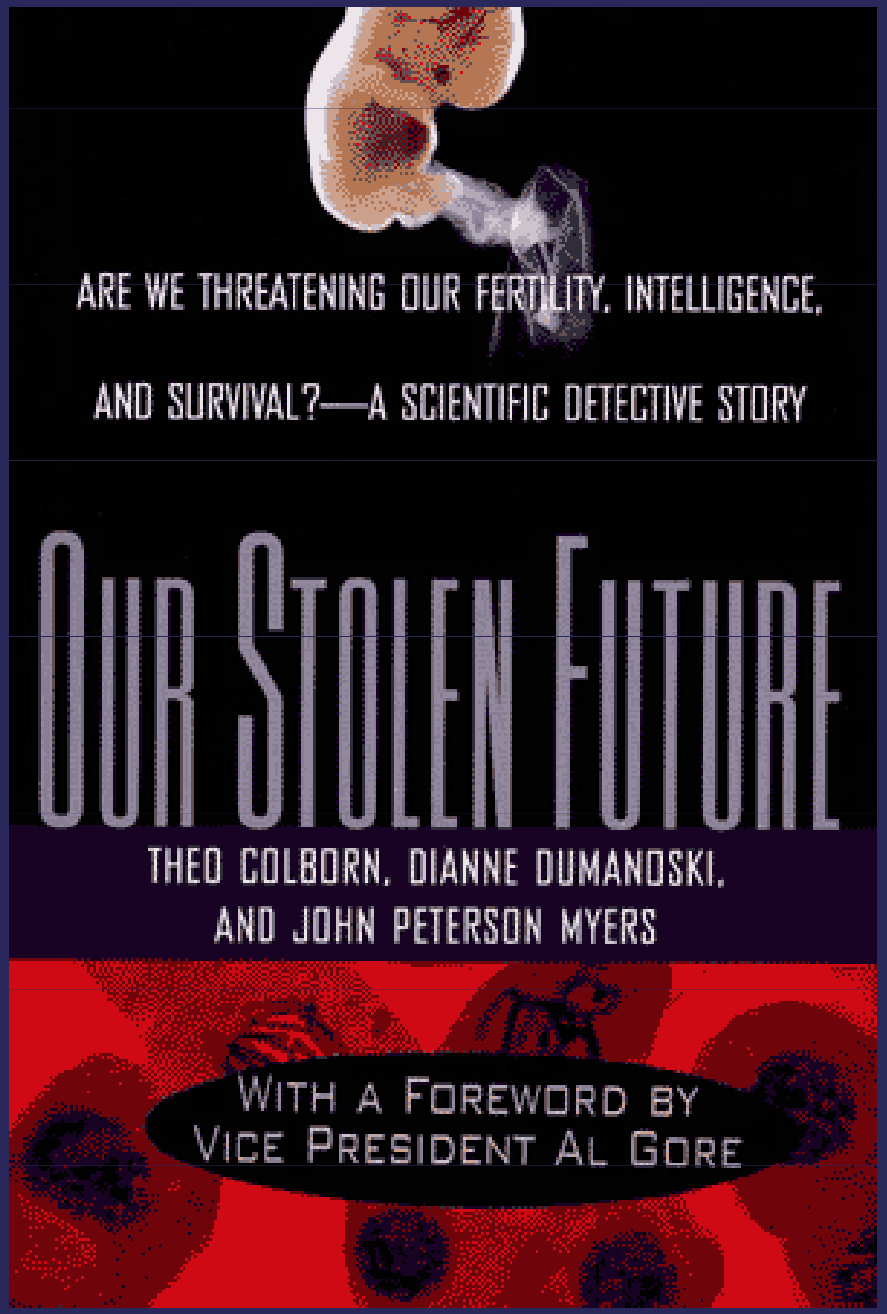
- **poznání** interakcí mezi živými organismy a chemickými/toxickými látkami v prostředí na všech úrovních
- **využití poznatků pro racionální ochranu** živých organismů, jejich populací, společenstev a ekosystémů před chemickým znečištěním

Hlavní motivace výzkumu toxických látek?

! ČLOVĚK !

- *Rats exposed in the womb* **to a single low dose of a widespread brominated flame retardant become hyperactive and have decreased sperm counts…**





news@nature.com
The best in science journalism

Published online: 21 October 2005; | doi:10.1038/news051017-16

Pollution makes for more girls

The stress of dirty air skews sex ratios in Sao Paulo.

Erika Check

Toxic fumes favour the fairer sex, a group of researchers in Brazil has found.

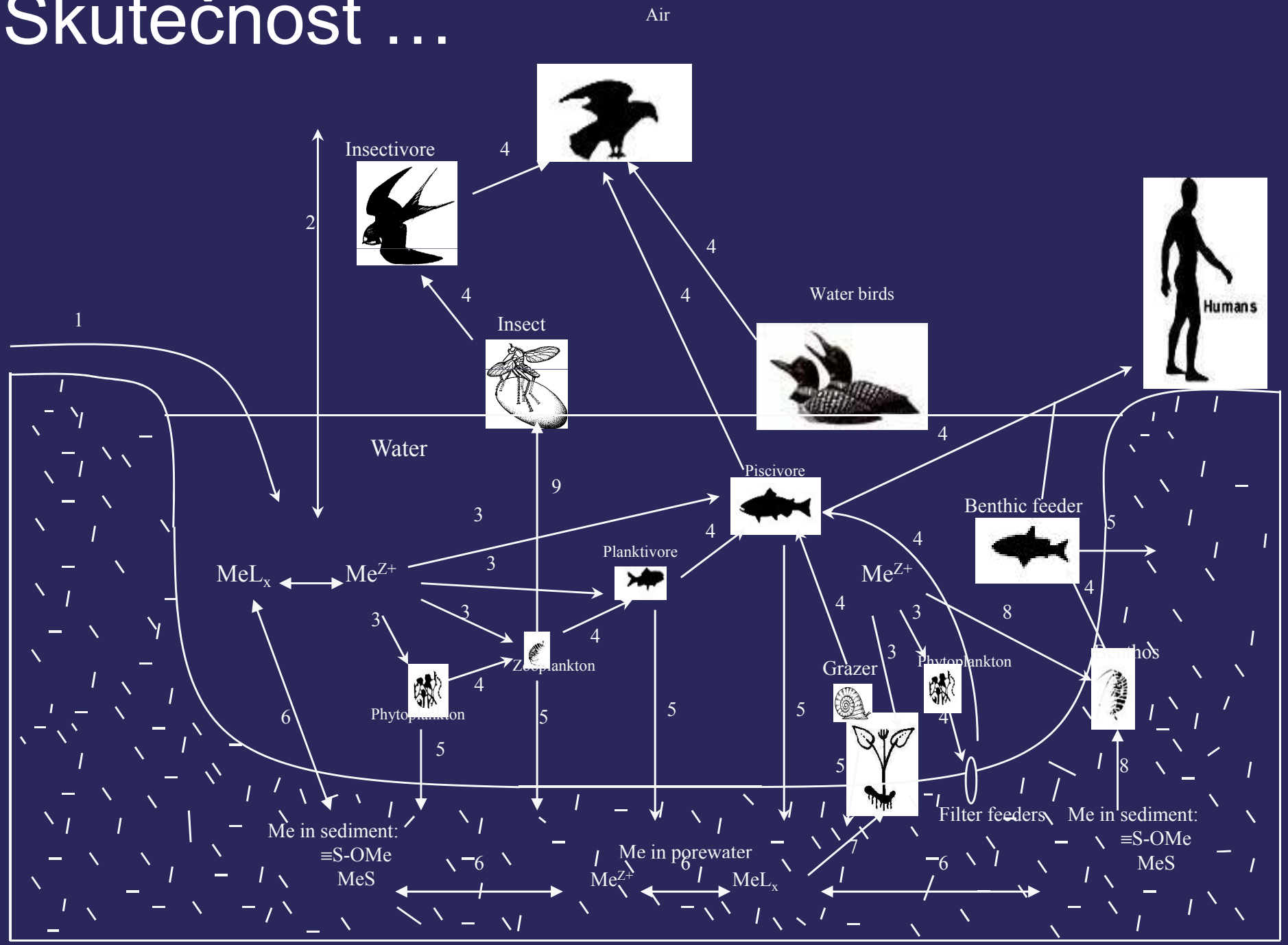
Babies born in highly polluted areas are more likely to be girls.

© *Alamy*

Jorge Hallak and his team at the University of Sao Paulo turned up the surprising result by studying babies born in their city. They divided the metropolis of 17 million people into areas of low, medium and high air pollution, using test results from air-quality monitoring stations. They then studied birth registries of children born from 2001 to 2003.

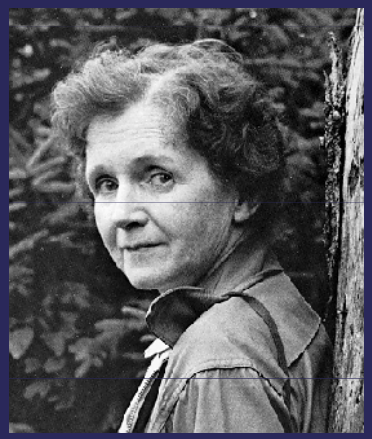
The team found that 48.3% of babies were female in the least polluted areas, but 49.3% were female in the dirtiest parts of town. After measuring the ratio of boys to girls born in all the areas, they calculated that 1,180 more babies would have been boys in the polluted areas if they had the same sex ratios as the cleaner areas. The team reported their findings on 17 October at the American

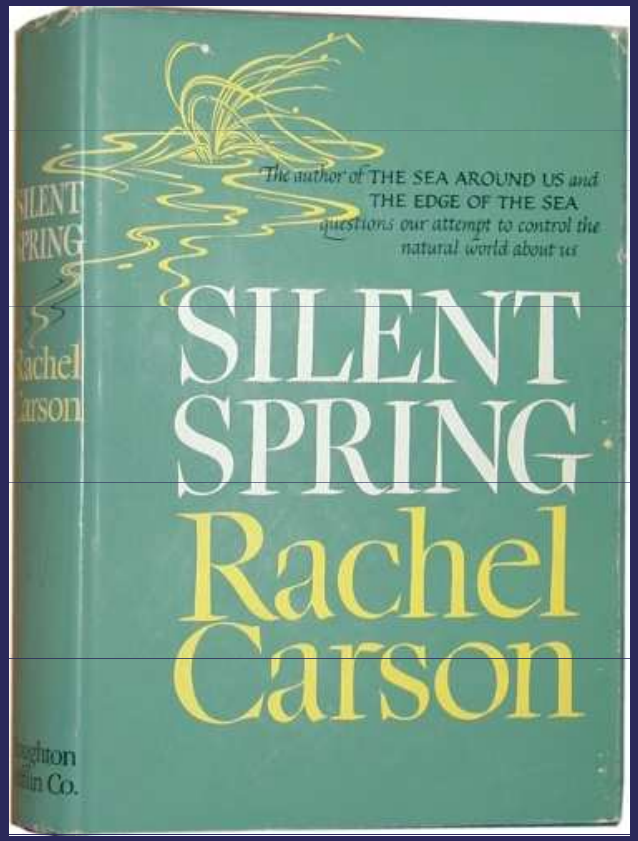
Skutečnost …

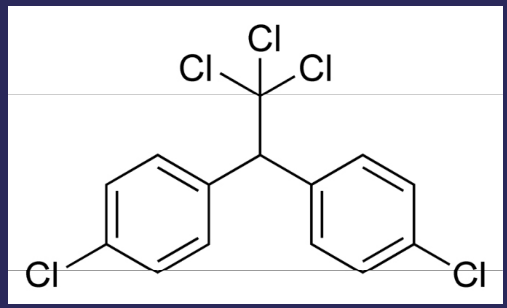

Air
Insectivore
Insect
Water birds
Humans
Water
Piscivore
Benthic feeder
Planktivore
MeL$_x$
Me^{Z+}
Me^{Z+}
Zooplankton
Phytoplankton
Grazer
Phytoplankton
Filter feeders
Me in sediment:
≡S-OMe
MeS
Me in porewater
Me^{Z+}
MeL$_x$
Me in sediment:
≡S-OMe
MeS

Složitost (eko)systému
= složité problémy a komplikace …

1962

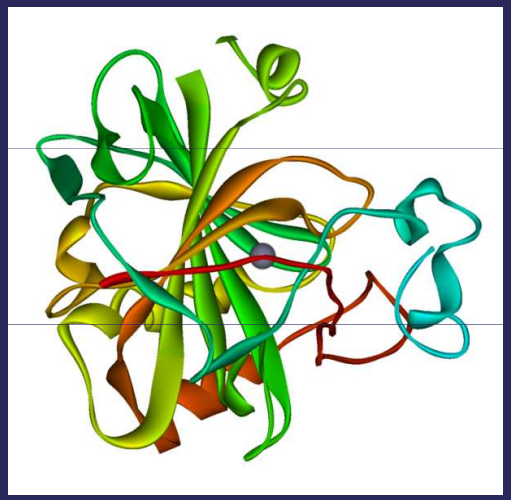




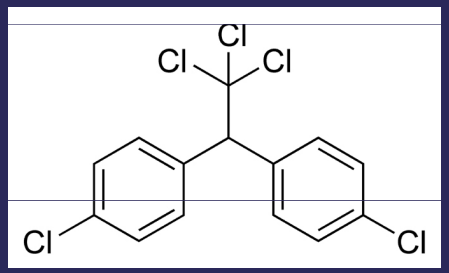


http://www2.ucsc.edu/scpbrg/

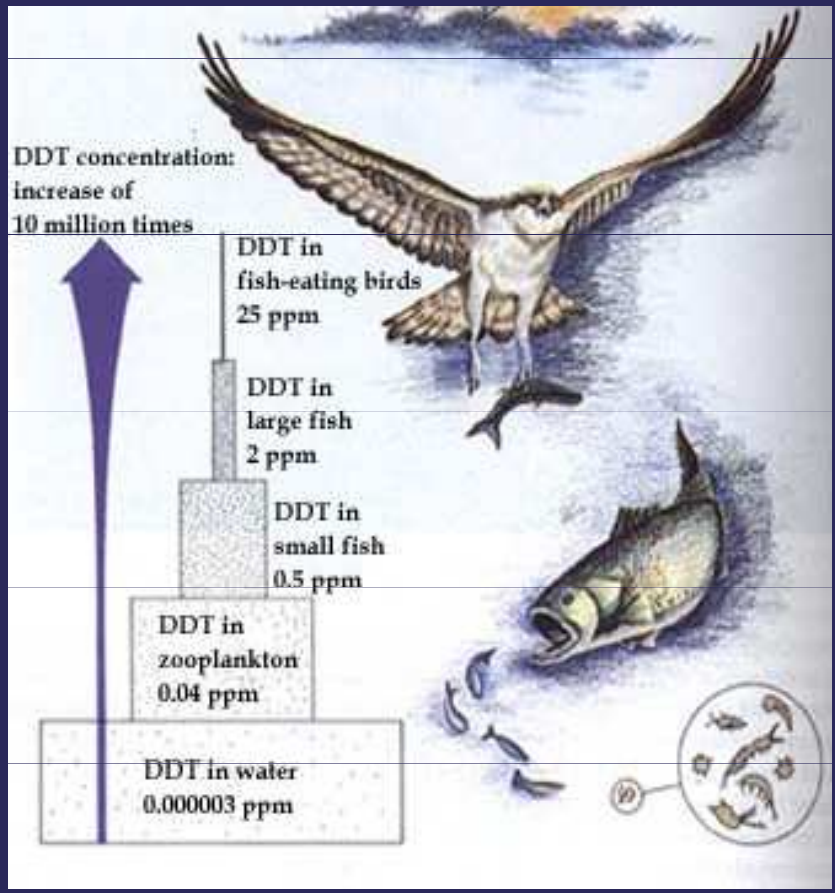
Bitman et al. *Science* 1970, 168(3931): 594



Biochemie:
ptačí karbonátdehydratáza



In situ: bioakumulace
-> úbytek populací ptáků



In vivo: měknutí vajíček

Environmental (chemical) problems

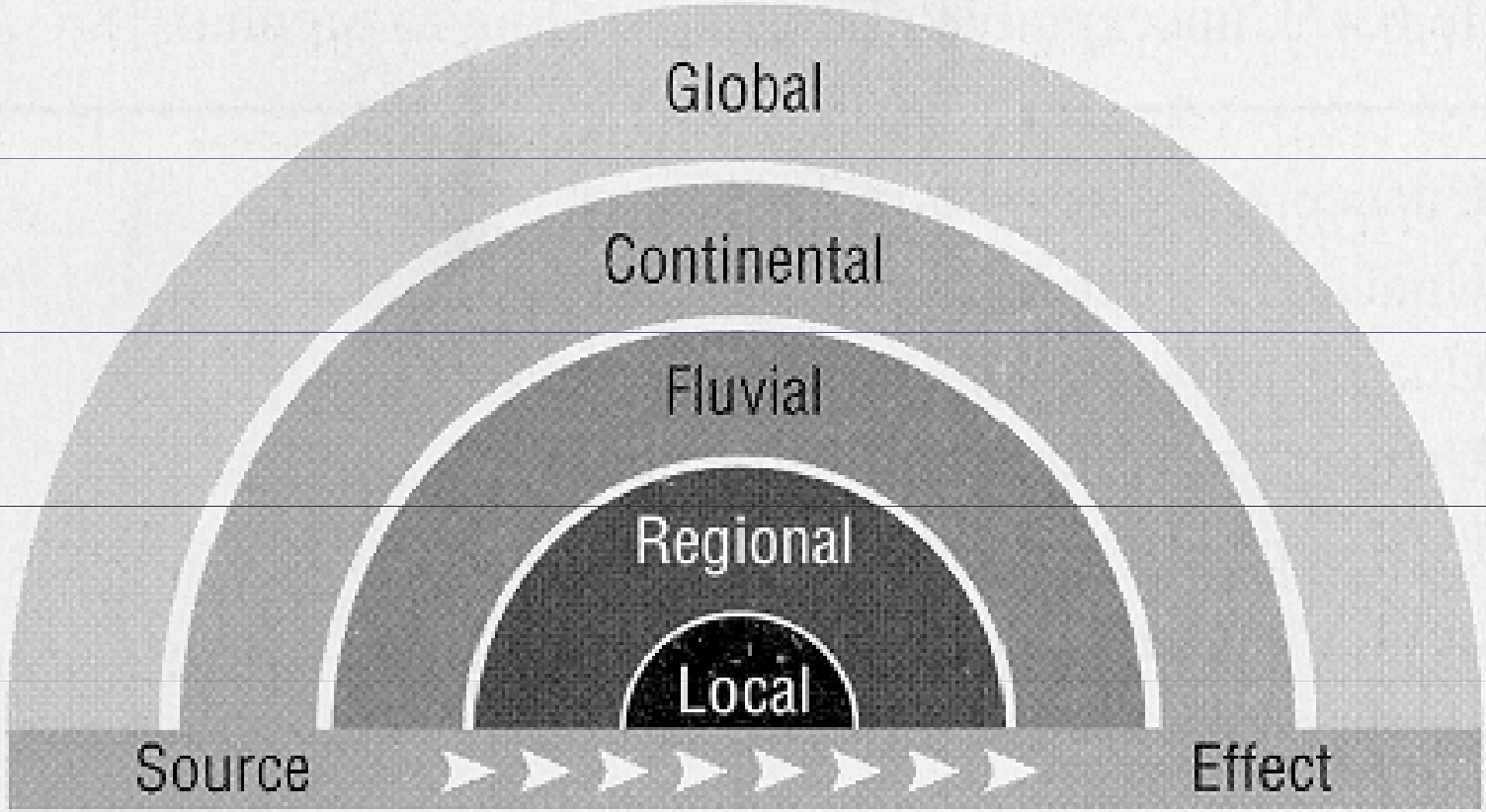


Figure 6.2. Five levels of scale at which environmental problems occur [9].

Hlavní teze:

Rozlišíme bezpečné a nebezpečné chemické látky

- bezpečné budeme používat
- nebezpečné budou zakázány

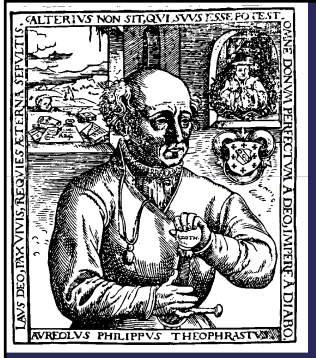
Definice bezpečnosti ?

Paracelsus (1493 - 1541)

'What is there which is not a poison?

- *All things are poison and nothing without poison.*

- *Solely the dose determines that a thing is not a poison.*

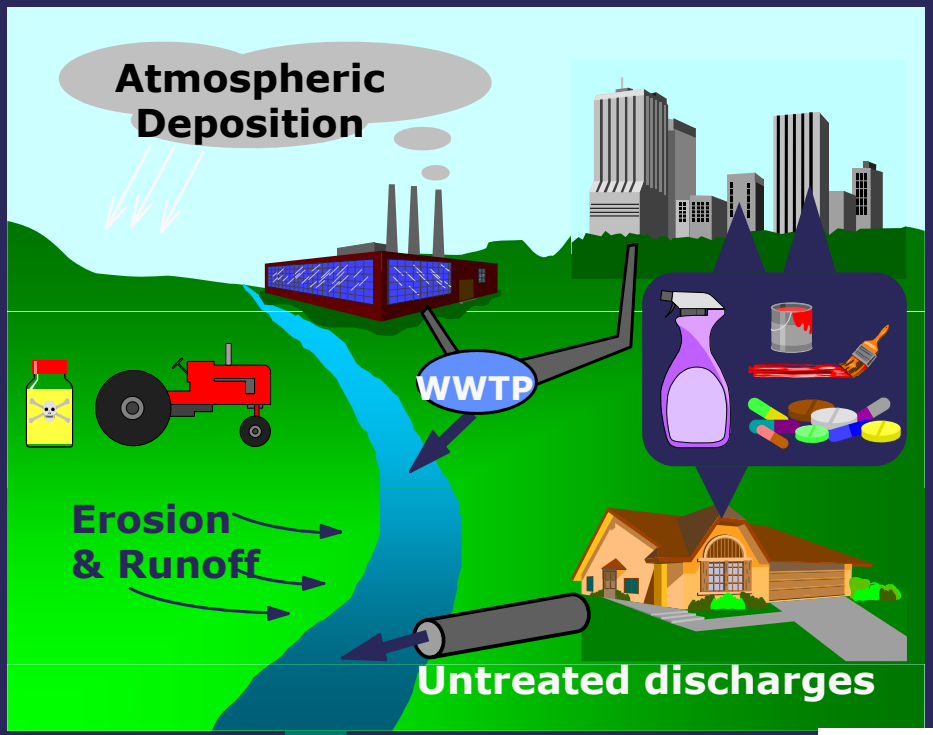


Příčina -> Důsledek
Dávka -> Účinek

-> Risk assessment = Hodnocení rizik

EUSES European Union System for the Evaluation of Substances

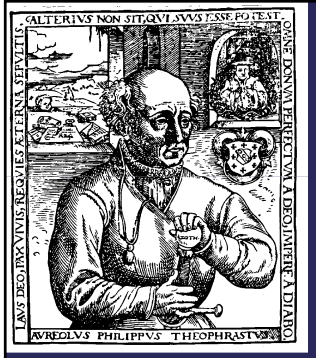
Expozice (dávka)



Efekt

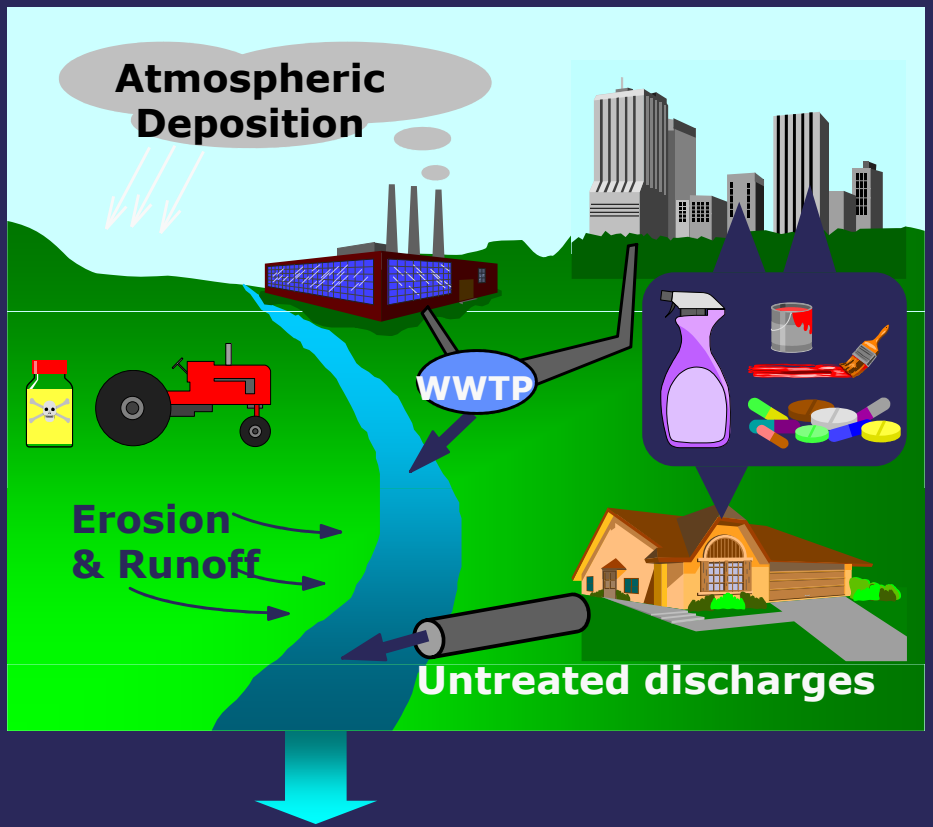
(Jaká expozice vyvolá efekt ?)

Laboratorní a polní studie
Ekotoxikologické testy



Jak poznat dávku (expozici) ?

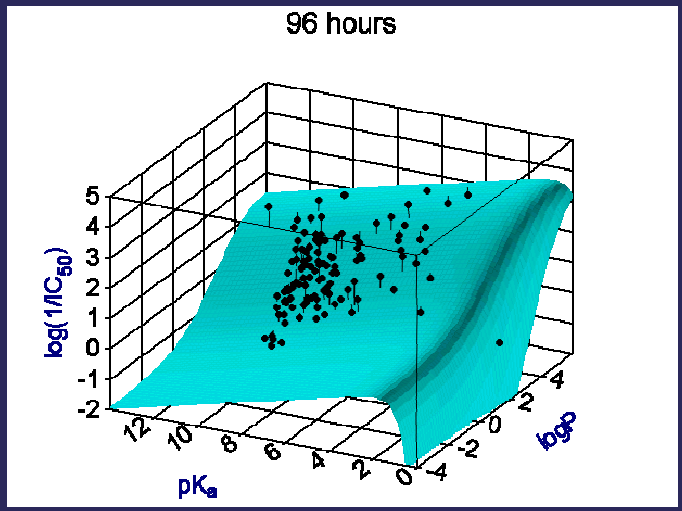
Expozice (dávka)



Jak poznat, zda je látka „bezpečná“?

PŘEDPOVĚDI
As, Hg …

akutní toxicita pro ryby
log (1/LC50) = 0.907 . log **Kow** - 4.94

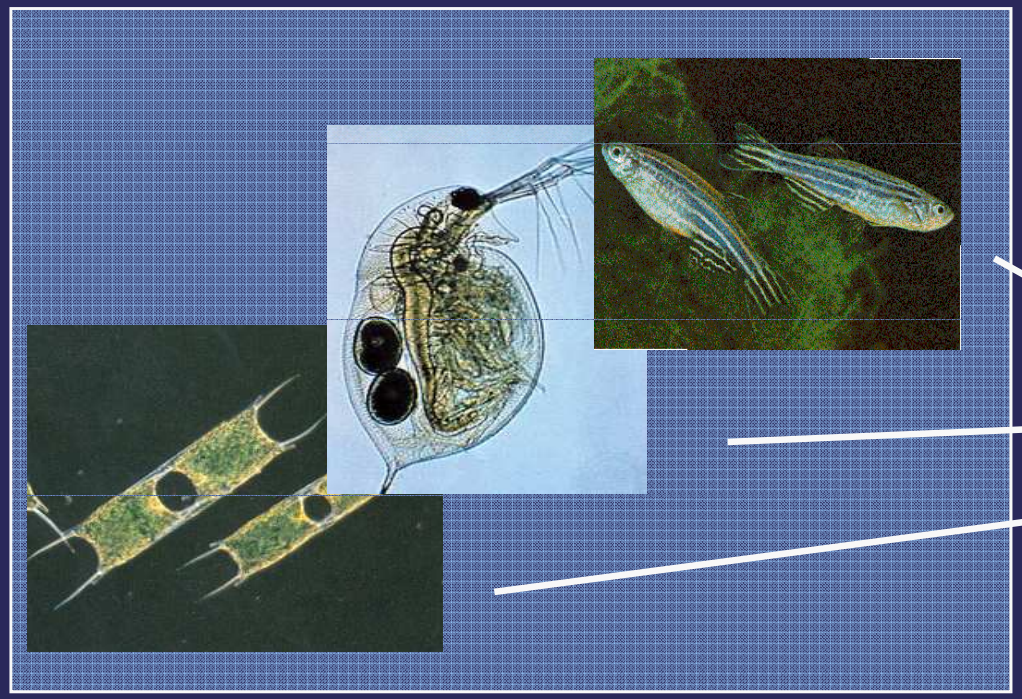


TESTOVÁNÍ

- toxicita

- ekotoxicita

Hodnocení účinků (ekotoxikologické testy)



Cu addition

Concentration:

0.0 µg/L	13 µg/L	25 µg/L	50 µg/L	100 µg/L	200 µg/L
Control	1	2	3	4	5

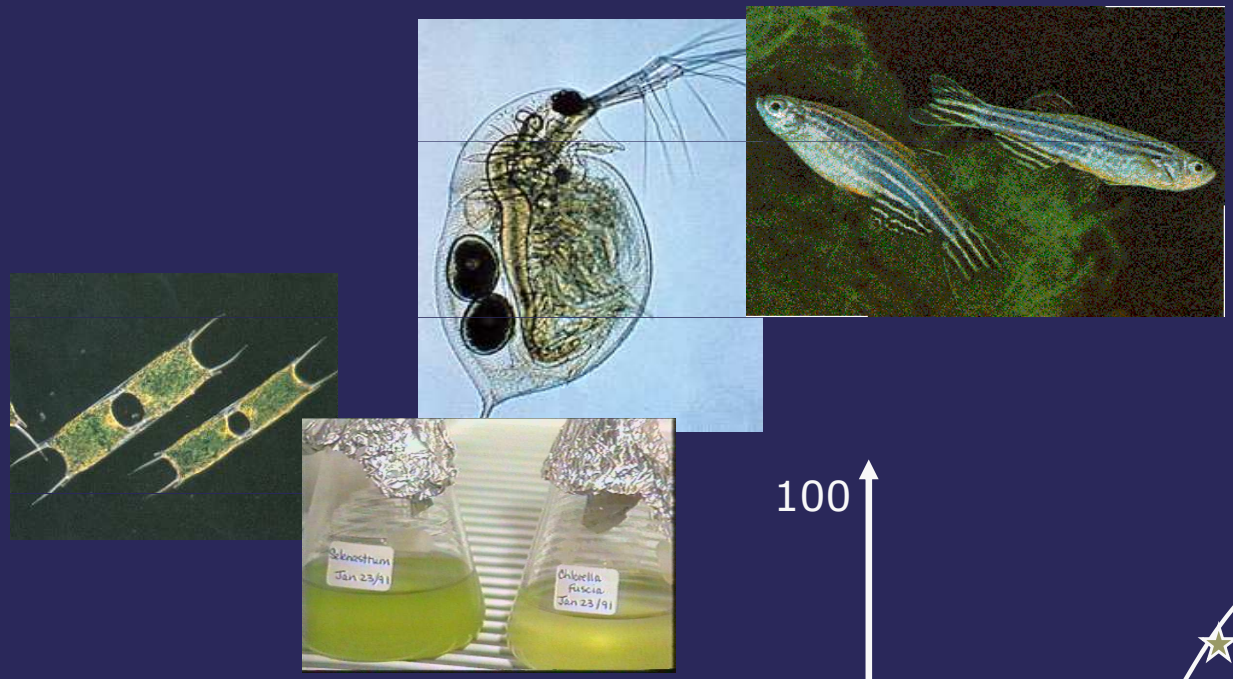
96-hour LC50 = 50 µg/L

Effect concentrations expressed in total/dissolved Cu

Extrapolation =

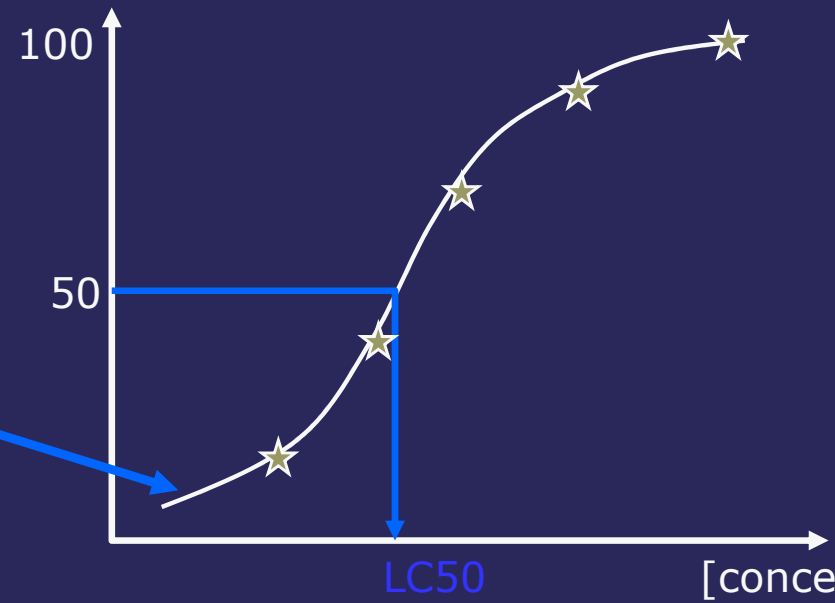
PNECs or EQCs expressed in total / dissolved Cu

Hodnocení účinků - výsledek

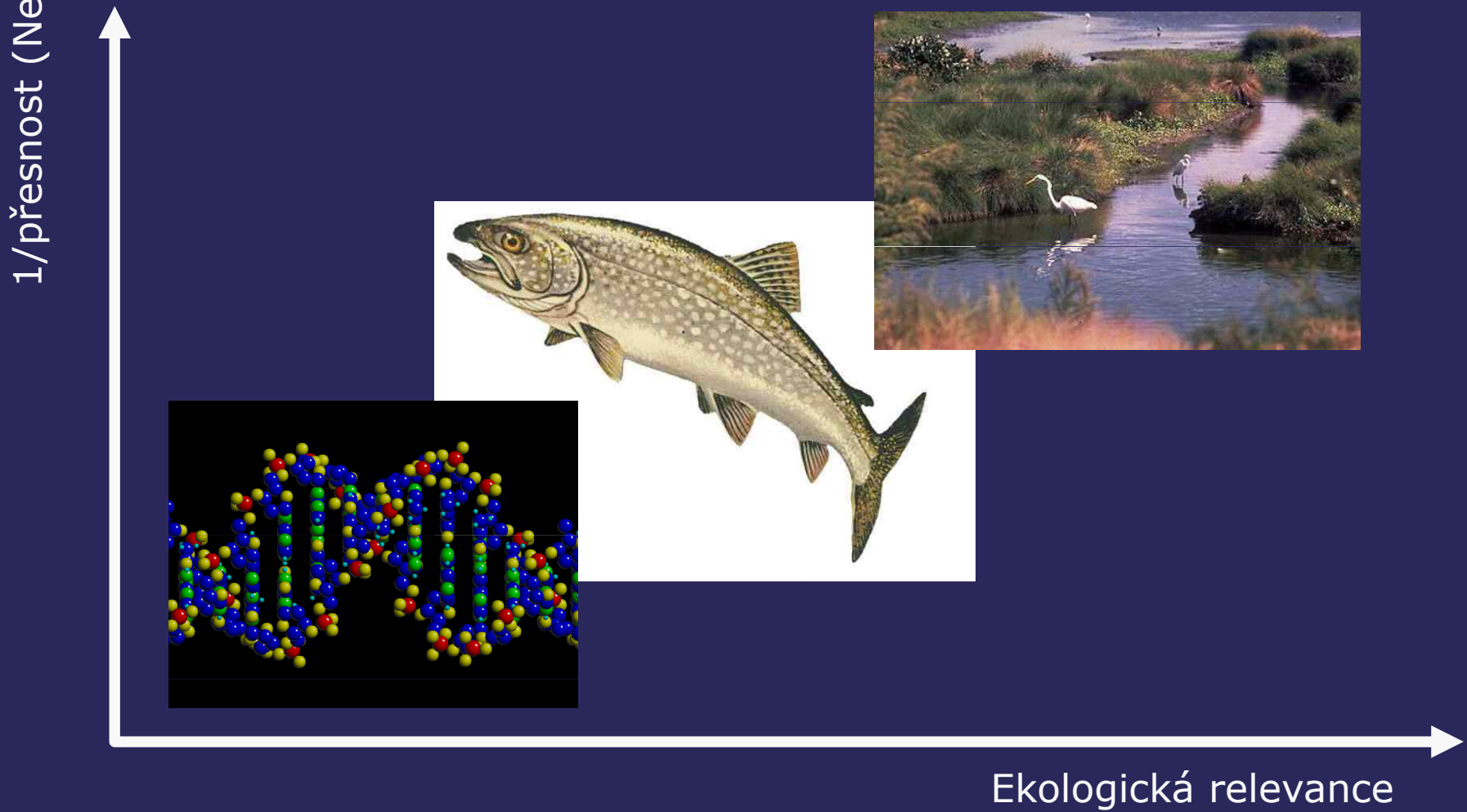


Threshold:

No Observed Effect Concentration (NOEC)



Ekotoxikologické výsledky vs. realita (ekosystémy?)



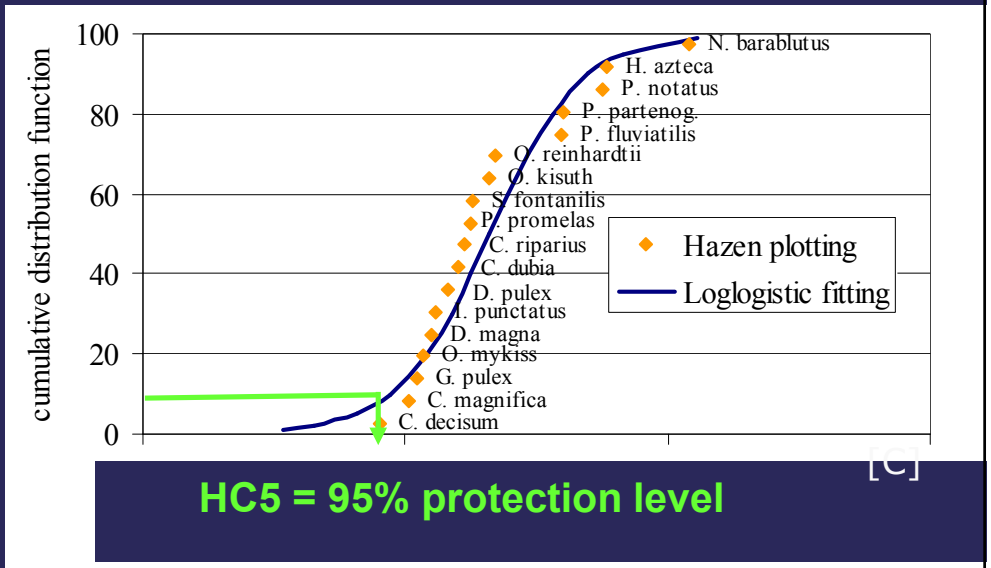
Využití výsledků -> bezpečná dávka ?

Hodnoty ekotox. EC50

Extrapolace

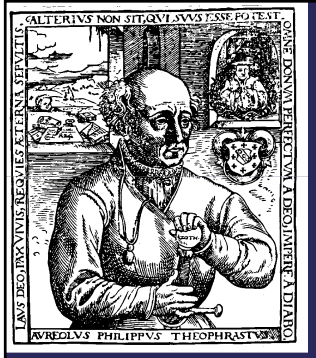
Data	Assessment factor
L(E)C50 short-term toxicity tests	1000
NOEC for 1 long-term toxicity test	100
NOEC for additional long-term toxicity tests of 2 trophic levels	50
NOEC for additional long-term toxicity tests of 3 species of 3 trophic levels	10

Species sensitivity distribution (SSD)



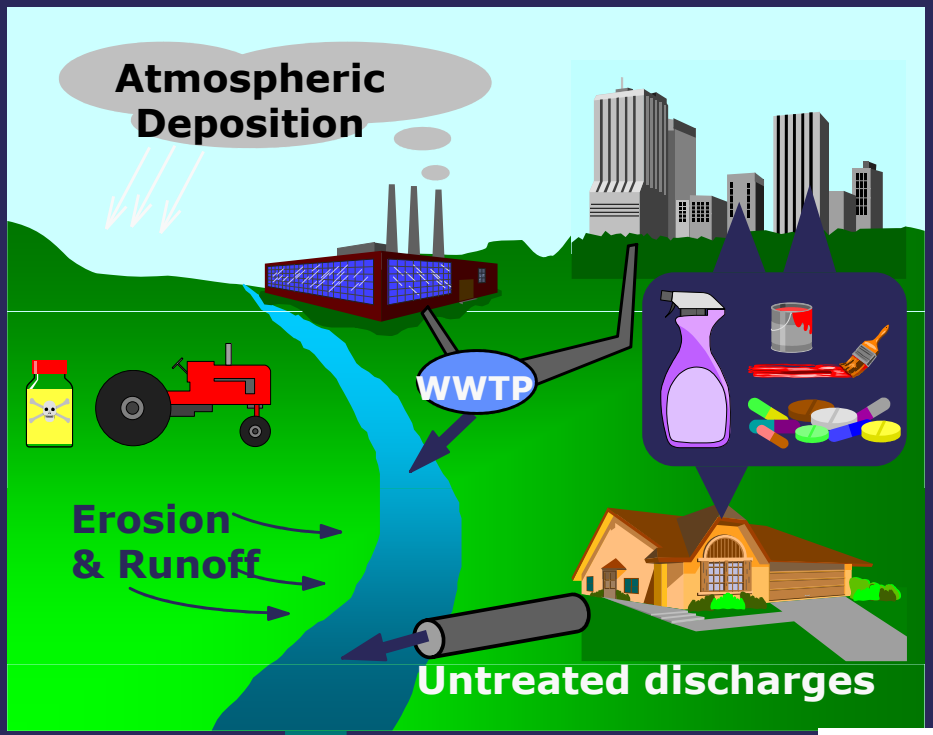
HC5 = 95% protection level

PNEC



VYHODNOCENÍ RIZIKA

Expozice (dávka)



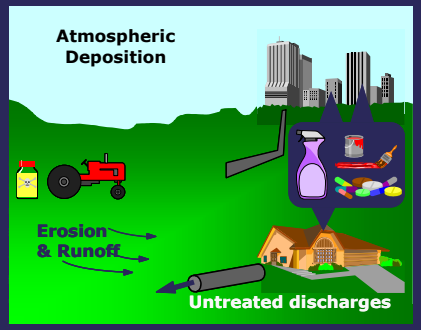
Efekt

(Jaká expozice vyvolá efekt ?)

Laboratorní a polní studie
Ekotoxikologické testy

Charakterizace rizika

EUSES European Union System for the Evaluation of Substances



Definice nebezpečnosti

EXPOZICE

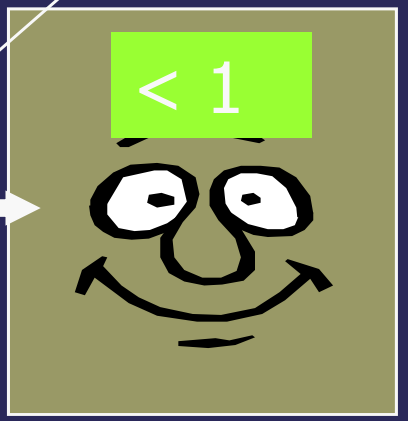
PEC

ÚČINEK

PNEC

RIZIKO ?

PEC/PNEC



Realita = limity:

Tabulka 1. pokračování

Kritéria znečištění vody (v µg/l, pokud není uvedeno jinak)						
	Metodický pokyn - podzemní voda			pitná voda	povrchová voda	
Ukazatele	A	B	C	ČSN 757111	vodár.	ostatní
VII. Chlorované alifatické uhlovodíky						
jednotlivé mimo násl.	0,1	50	100			
1,2-dichlorethan	0,1	25	50	10		
1,1-dichlorethen	0,1	10	20	0,3		
1,2-dichlorethenv	0,1	25	50			
dichlormethan	0,1	15	30			
tetrachlorethen	0,1	10	20	10		
tetrachlormethan	0,1	5	10	3		
trichlorethen	0,1	25	50	30		
trichlormethan	0,1	25	50	30		
chlorethen (vinylchlorid)	0,1	10	20	20		
VIII. Ostatní uhlovodíky (směsné, nehalogenované)						
NEL	50	200	1000	50	50	200
IX. Ostatní aromatické uhlovodíky (halogenované)						
PCB (suma 28, 52, 101, 118, 138, 153 a 180)	0,01	0,25	1	0,05	(d)	0,025
PCDD/PCDF (dibenzodioxiny a dibenzodifurany) v ng/l	*0,01*	*0,025*	*0,05*			
X. Ostatní						
Anorganické látky						
B	100	500	5000		300	500
Cl^-	25000	100000	150000	100000	150000	350000
F (F^- pro vodu)	250	2000	4000	1500	1000	1500
NH_4^+	120	1200	2400	500	1000	3000
NO_3^-	25	200	400	100	100	200
S (sulfidická)	10	150	300		(d)	20
volné kyanidy/thiokyunáty	5	40	75			
komplex. kyanidy (pH<5)	10	250	500			
komplex. kyanidy (pH>5)	10	100	200			
Organické látky						
cyklohexanon	0,1	250	500			
ftaláty (suma)	1	5	10			
hydrochinon	0,1	400	800			
pyrokatechin (katechol)	0,1	600	1200			
kresoly	0,1	100	200			
pyridin	0,1	3	6			
resorcin (resorcinol)	0,1	300	600			
tetrahydrofuran	0,1	5	50			
tetrahydrothiofen	0,1	15	30			
trinitrotoluen (TNT)	0,1	0,5	1			
tenzidy aniontové (PAL-A)	20	250	500	200	200	1000

Limity ???

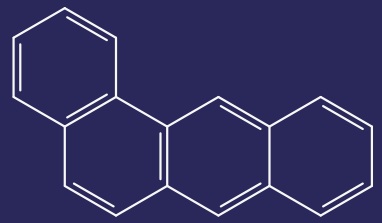
- Pro které matrice existují limity?

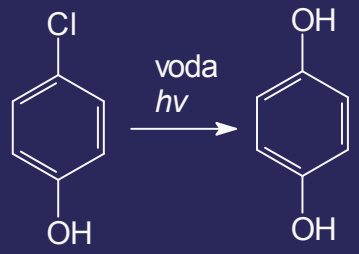
- Pro které látky existují limity?

Matrice 1:
- Ovzduší (! Lidé)
- Potraviny (! Lidé)
- Léky (! Lidé)
- Pitná voda (! Lidé)
- Orná půda (! Lidé)

Chemické látky:
- PAHs
- chlorfenoly
- POPs
- tox. Kovy (As…)

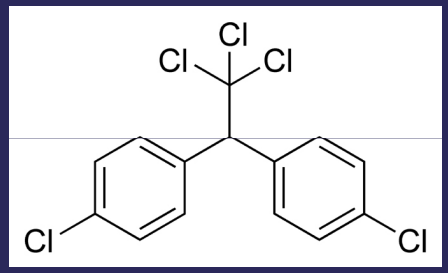
(formaldehyd …





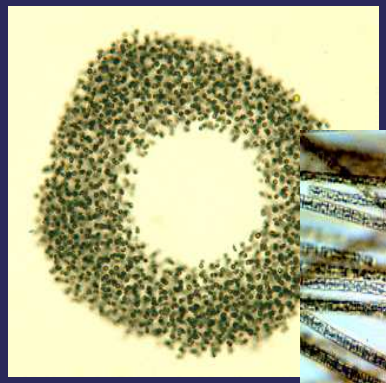
Matrice 2:
- povrchová voda
- odpadní vody
- pevný odpad

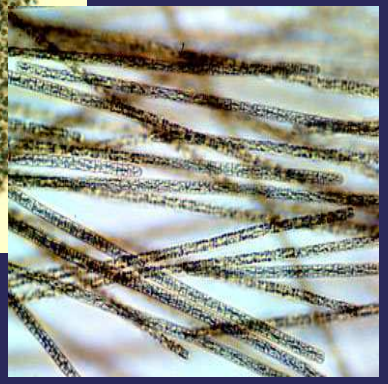
CHYBÍ … půda, sedimenty
+ PROBLÉM co dělat při překročení limitů?

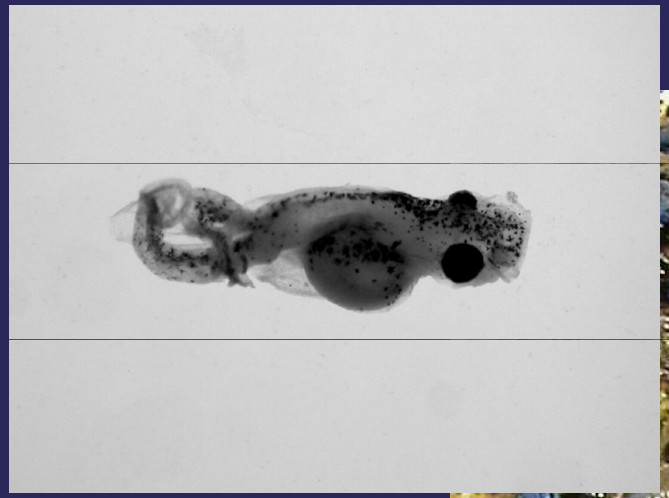


Složitost (eko)systému
= složité problémy a komplikace …

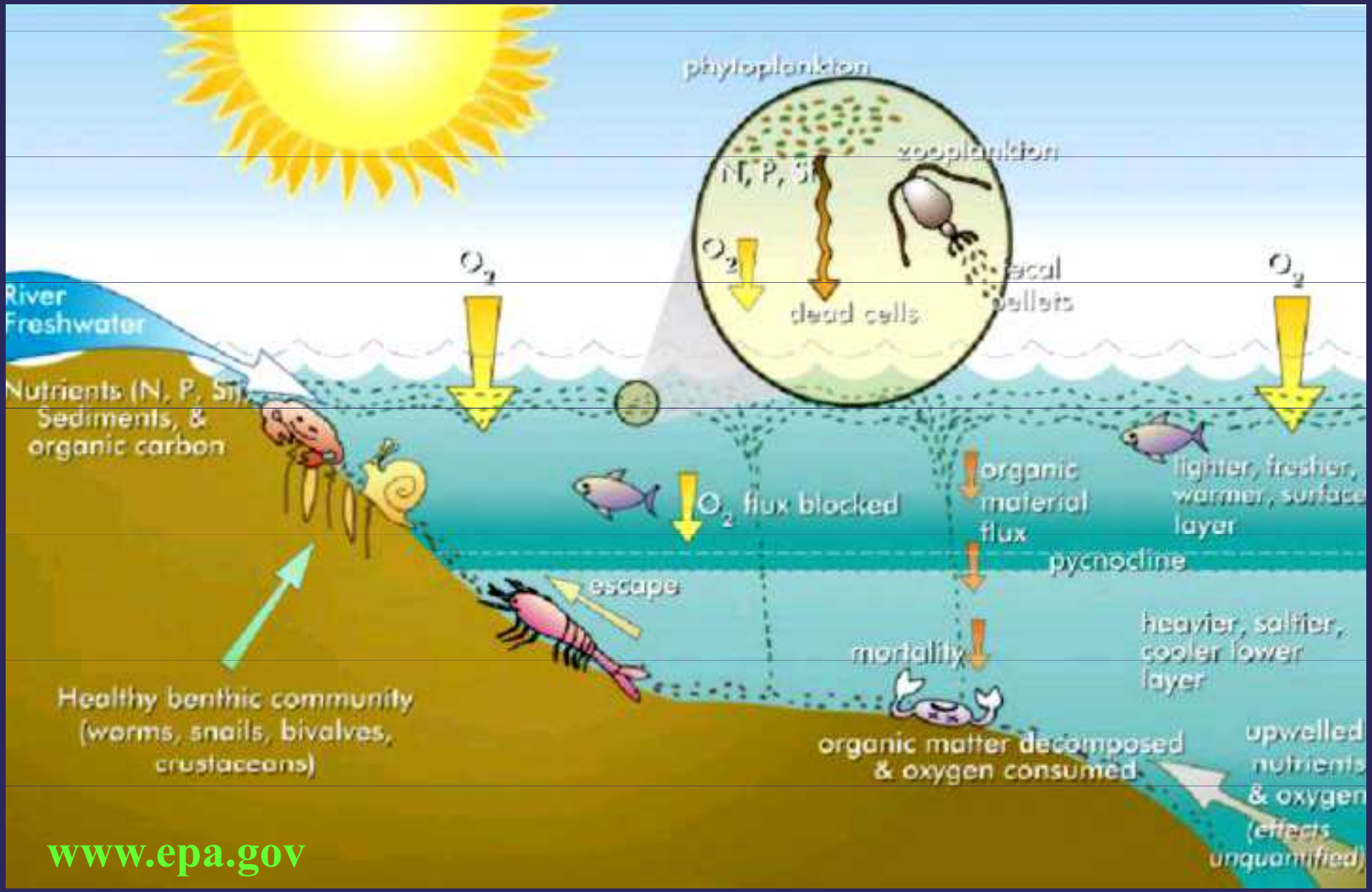
CHEMIKÁLIE V PŘÍRODĚ …
a organismy … „toxicita není jen smrt“





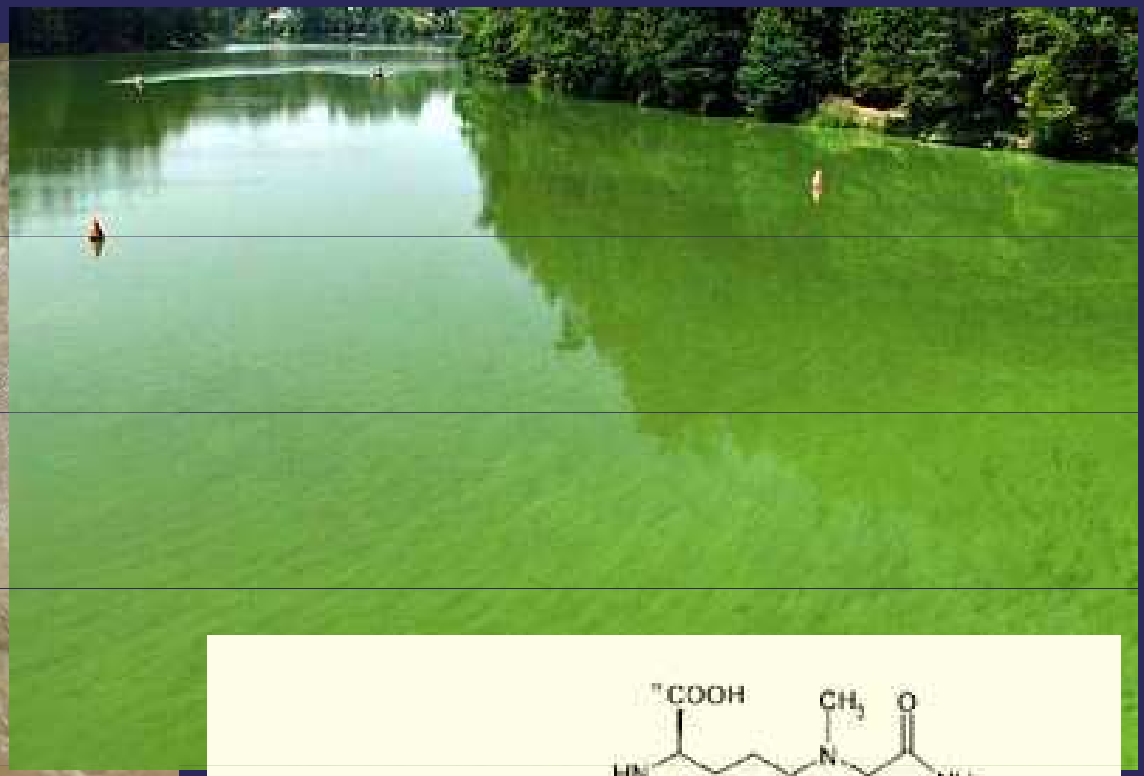


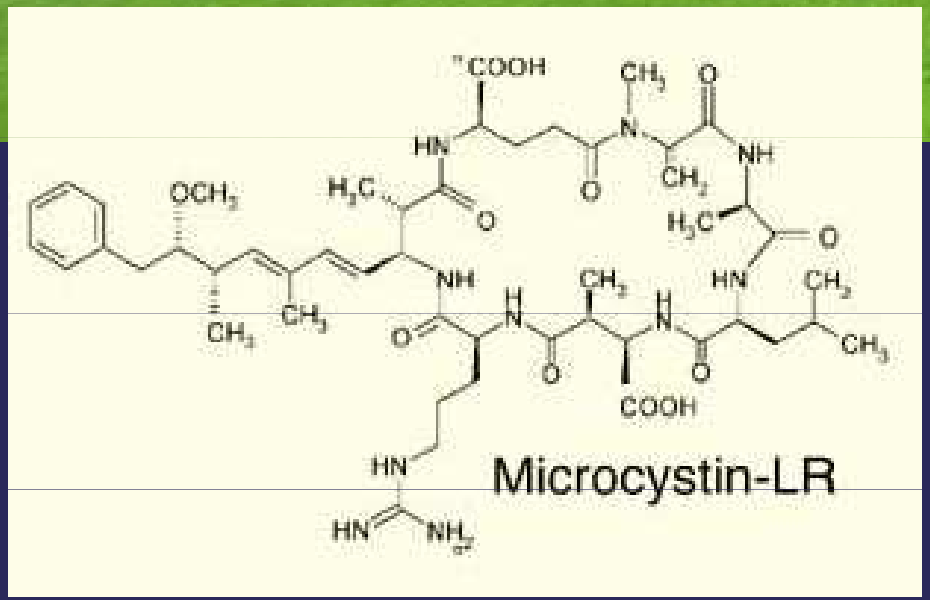
Živiny … jsou nebezpečné?



www.epa.gov

Chemikálie a **ne**přímá toxicita … sinice

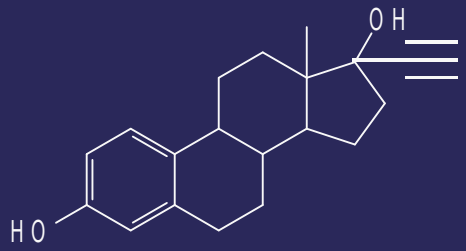


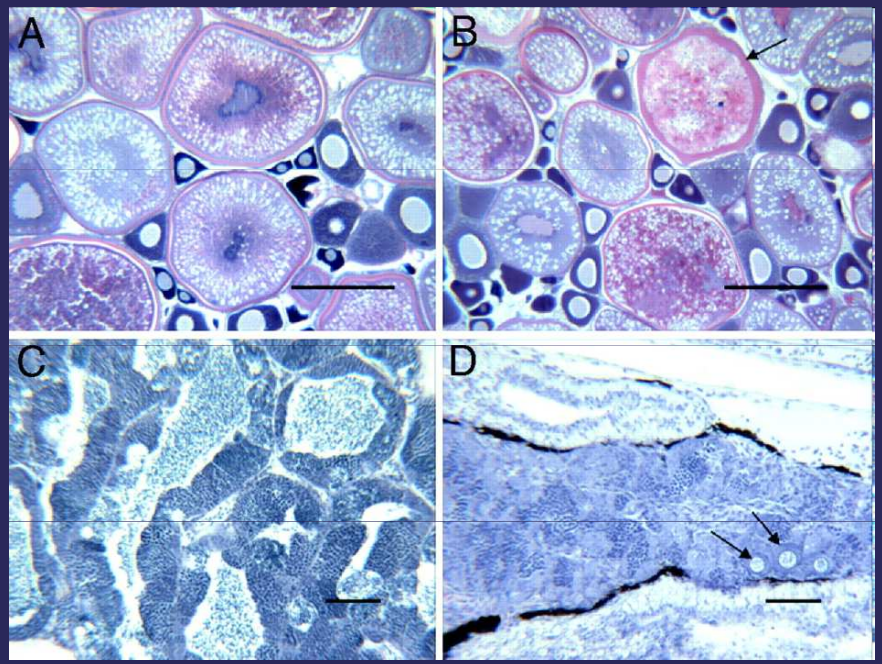


www.wikipedia.com

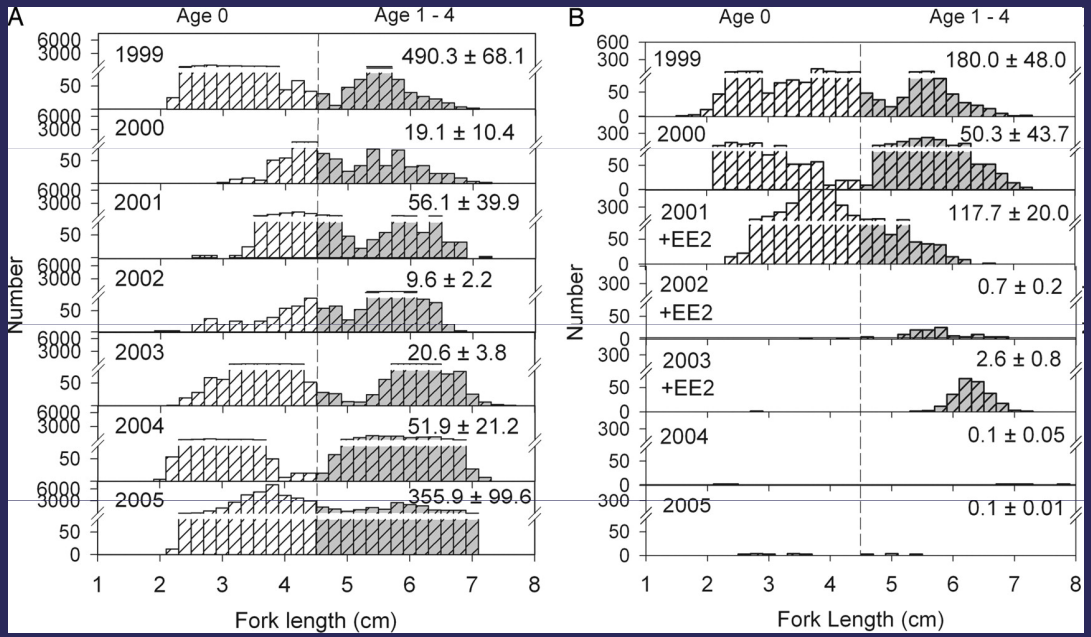
Kidd, K.A. et al. 2007. **Collapse of a fish population** following exposure to **a synthetic estrogen**. *Proceedings of the National Academy of Sciences* 104(21):8897-8901

5 ng/L (!)
7 years

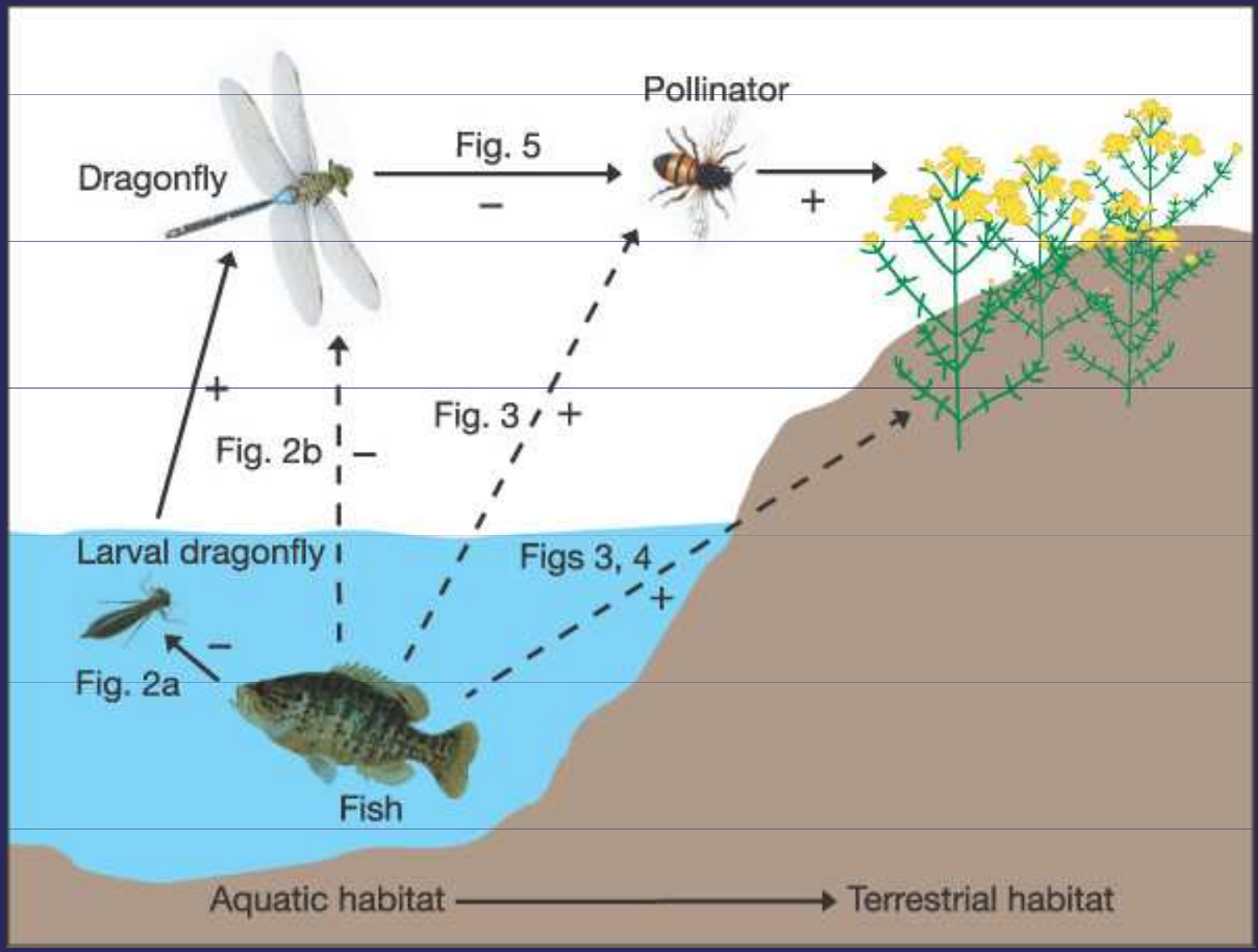




Controls **+Ethinylestradiol**



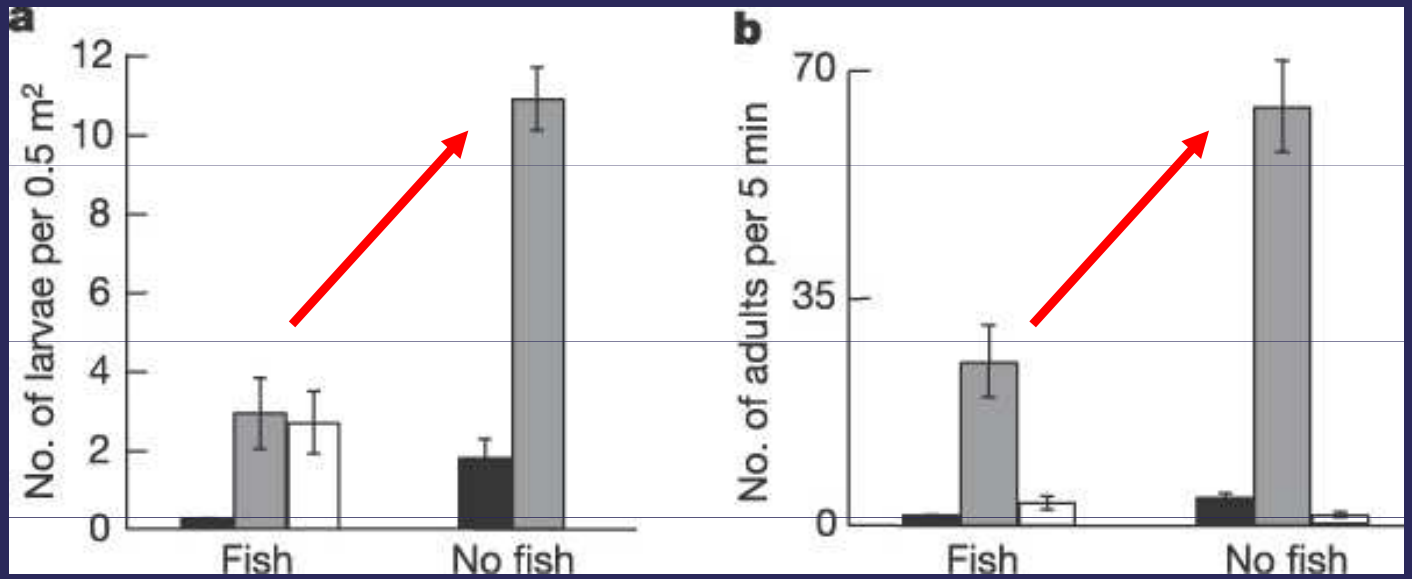
- **ECOLOGY vs ECOTOXICOLOGY**
  - Key / Keystone species
    - dramatic changes in all community – example: FISH !



Knight et al., NATURE (2005) 437: 880

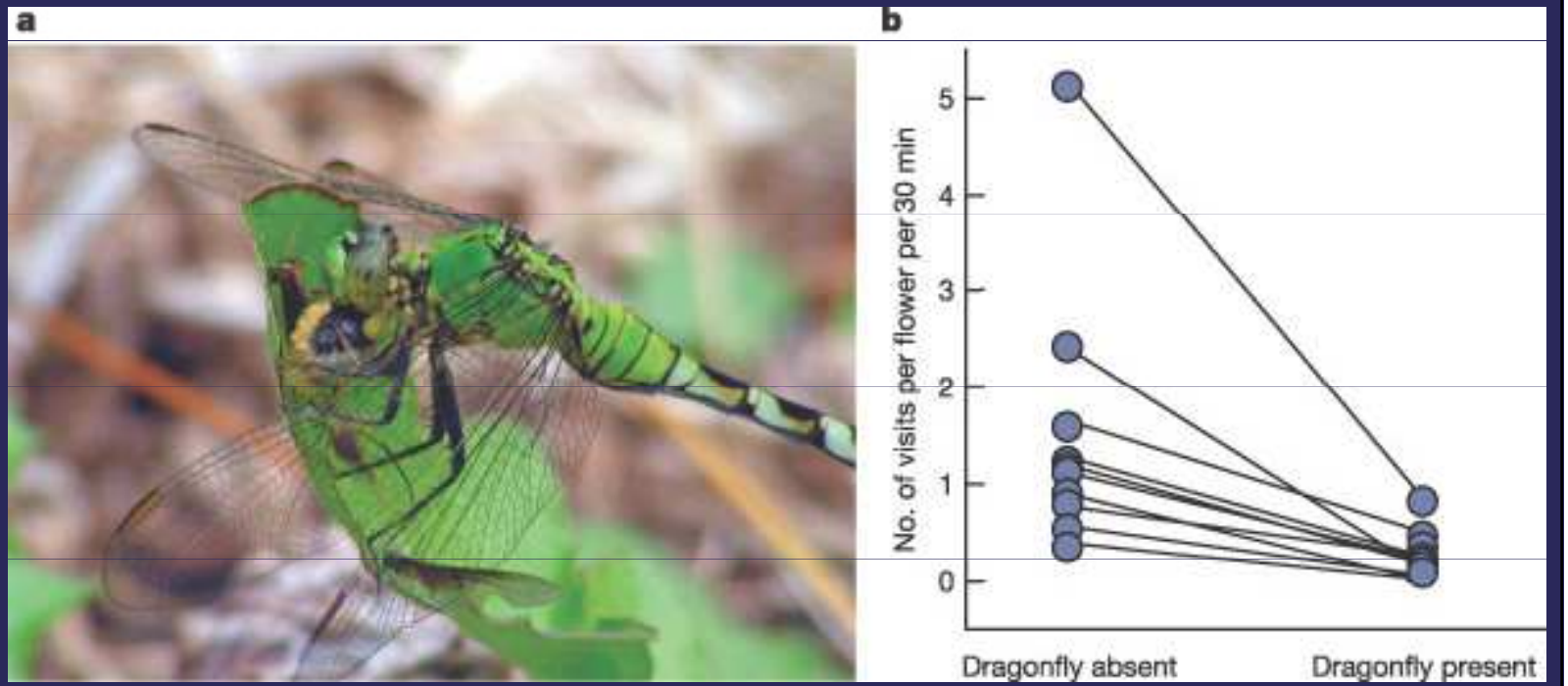
Knight et al., NATURE (2005) 437: 880

No. of dragonflies
3 size categories
(small/med/large)



„Plant reproduction"

(pollination activities of bees)



Toxické chemikálie a globální problémy ?

Promíchávání oceánů

-> fungování zeměkoule

[Nature 447, p.522, May 31, 2007]

Mořský život přispívá až 50% k mechanické energii nutné k promíchávání oceánů !

[Dewar, Marine Res 64:541 (2006)]

Souhrn 1:
„toxické chemikálie současnosti“
(o kterých víme …)

- **Veterinární léčiva**
- **Humánní léčiva**
- **Zhášeče hoření**
- **Aditiva (ftaláty)**
- **Komunální chemie**
- **Částice**
- **Nové materiály („nano“)**

PRAKTICKY …
Můžeme problém toxických látek vůbec regulovat ?

REACH

EU and risk assessment

- **± 40 Directives** or Regulations concerning the evaluation and management of the dangers/risks associated with chemical substances
  - Regulation EEC 793/93 – **Existing substances**
  - Directive 67/548/EEC – **New substances**
  - Directive 98/8/EC - **Biocides**

EU and risk assessment

Existing substances

- 100196 substances in EINECS
- 2747 HPVCs (Allanou et al., 1999)
  - 14% minimum data-set (base-set)
  - 65% less than base-set
  - 21% no toxicity data
- Priority lists

- Situation in 2005 (after 10 years)
  - 141 substances RA status
  - 74 draft RAR
  - **48 final RAR**

EU and risk assessment

Conclusions on current systems

- **Too slow**
- **Insufficient data** for most substances:
  - Performing RA
  - Development of risk reduction measures
- Possibly: **inadequate protection**

EU now & future: **REACH**

Registration, Evaluation and Authorisation of Chemicals

- 27-2-2001: White Paper on the Strategy for Future Chemicals Policy
- 23-10-2003: Commission's proposal REACH

European Chemicals Agency
(echa.europa.eu)

REACH : Registration, Evaluation and Authorisation of CHemicals

Registration

>1 tonne:
Manufacturer/
importer gathers on
- properties
- identified uses
- safe management

European Chemicals Agency

Most substances:
No further action

No further action

Evaluation

Industry can be asked for more info

Safety info to public

Safety info to clients

Member States/Agency

Dossier evaluation
- of animal testing
- of compliance

Substance evaluation
- suspicion of risks

Substance needs to be regulated further

Information to be used under other EU legislation	It poses unacceptable risks	It has very hazardous properties

No authorisation: Use is not considered to be adequately controlled

Authorisation is granted by the Commission

No authorisation: Benefits are too small compared to risks/suitable substitutes are available

Risk assessment is reviewed

Socio-economic benefits and possibility for substitution are weighed against risk

Industry says will be adequately controlled

Industry says will not be adequately controlled

Authorisation*

The substance is a CMR** a PBT** or a vPvB** or has an equivalent serious and irreversible effect and should not be used without authorisation.

Restrictions* by the Commission

Based on Member States, the Commission can decide on risk management, ban certain uses, or ban substances altogether.

* Substances do not have to be registered or evaluated to be placed under authorisation or restriction. They can be identified in other ways.
** Can cause cancer or mutations, or is toxic to reproduction; or is persistent, bio-accumulative and toxic, or very persistent and very bio-accumulative.

REACH: aims & timing

- Protection of man and the environment
- Increase competiveness of EU chemical industry
- Increase transparency
- Avoid fragmentation of market
- Integration with international policies
- Reduction use of test animals

- **30000 existing substances**
  - 0-3 year: all HPVC and CMR substances
  - 4-6 year: all 100-1000 t/y substances
  - 7-11 year: all 10-100 and 1-10 t/y substances

REACH: data type?

- Physico-chemical properties, e.g.:
  - Vapour pressure, boiling point, Kow,…
- Human toxicology, e.g.:
  - Acute and chronic toxicity, skin irritation, carcinogenity,…
- Environment/ **Ecotoxicological** information, e.g.:
  - Acute and/or chronic toxicity for aquatic organisms, biodegradation, …

REACH: how many substances

Table 6. Estimated testing needs (% of total number of substances)

Endpoint	Minimum	Average	Maximum
6.3 Skin sensitisation	7486 (25.5)	10293 (35.1)	13728 (46.8)
6.2 Eye irritation (incl. *in vivo*)	5923 (20.1)	6910 (23.5)	8182 (27.9)
6.4.4 *In vivo* mutagenicity study	6580 (22.4)	6580 (22.4)	6580 (22.4)
7.1.2 Growth inhibition algae	2638 (9.0)	5277 (18.0)	11466 (39.1)
7.1.4 Active sludge respiration test	4616 (15.7)	4616 (15.7)	4616 (15.7)
7.1.1 Short-term *Daphnia* toxicity	2321 (7.9)	4096 (14.0)	8798 (30.0)
6.1 Skin irritation/corrosion (incl. *in vivo*)	1974 (6.7)	3949 (13.4)	5817 (19.9)
7.2.2.1 Hydrolysis	2691 (9.2)	3425 (11.7)	4518 (15.4)
6.4.1 Gene mutation study in bacteria	875 (3.0)	2916 (9.9)	6424 (21.9)
6.4.2 Cytogenicity study in mammalian cells	875 (3.0)	2916 (9.9)	6424 (21.9)
6.7.2 Development toxicity study	2408 (8.2)	2893 (9.9)	3711 (12.6)
7.2.1.1 Ready biodegradability test	1574 (5.4)	2624 (8.9)	5752 (19.6)
6.7.3 Two-generation reproduction toxicity	1665 (5.7)	2135 (7.3)	2699 (9.2)

REACH (2005-today): how much data available?

	Phys. chem. properties	**Toxicological information**	**Ecotoxicological information**
1-10 t/y	**14**	**4**	**1**
10-100 t/y	**14**	**14**	**7**
100-1000 t/y	**17**	**19**	**18**
> 1000 t/y (HPVs ~ 2747)	**17**	**22**	**25**

REACH: costs

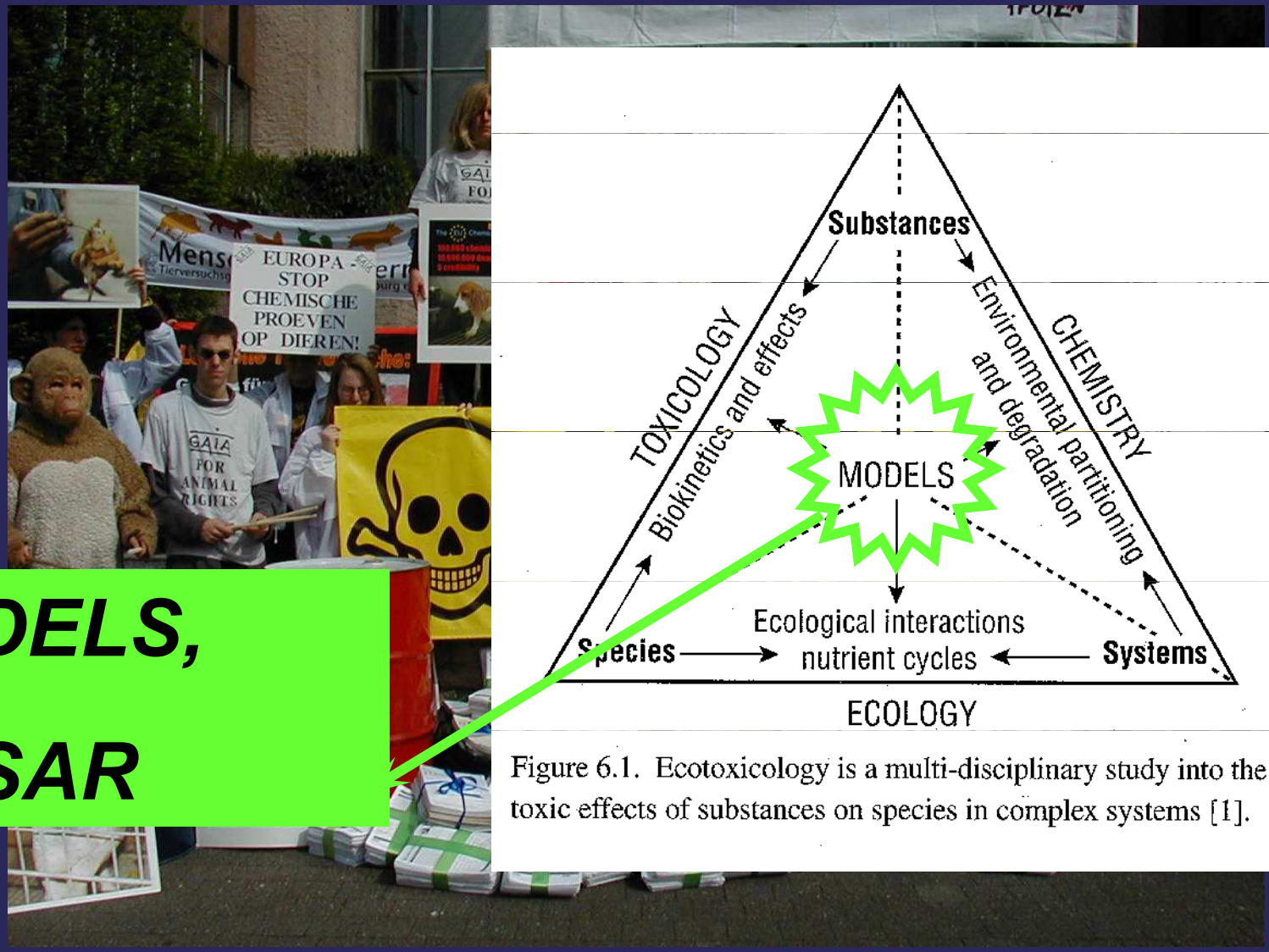
	>1t/y	>10t/y	>100t/y	>1000t/y	**Total**
Registration costs	€ 100 mn	€ 100 mn	€ 100 mn	€ 200 mn	**€ 500 million**
Testing costs	€ 150 mn	€ 300 mn	€ 350 mn	€ 450 mn	**€ 1250 million**
Safety data sheet costs					**€ 250 million**
Authorisation procedures					**€ 100 million**
Reduced costs for new substances below 1t etc.					**(benefit of € 100 million)**
Total testing and registration costs					**€ 2, 000 million**
Agency fees (paid by chemicals sector)					**€ 300 million**
Total costs (including Agency fees)					**€ 2, 300 million**

REACH: testing costs

Table 8. Estimated testing costs for most costly endpoints (Million EURO)

Endpoint	Minimum	Average	Maximum
6.7.2 Development toxicity study	396	476	611
6.7.3 Two-generation reproduction toxicity	293	376	475
6.4.4 *In vivo* mutagenicity study	129	129	129
6.6.2 Sub-chronic toxicity	76	111	210
6.6.3 Long-term repeated dose toxicity study (incl. 6.9 Carcinogenicity study)	44	52	73
6.6.1 Short-term repeated dose toxicity study	13	49	189
6.4.2 Cytogenicity study in mammalian cells	16	52	116
6.3 Skin sensitisation	29	40	54
7.2.1.1 Ready biodegradability test	19	32	71
7.3.2 Accumulation	14	28	67
7.1.2 Growth inhibition algae	13	26	57
6.7.1 Development toxicity screening	12	26	101
7.2.2.1 Hydrolysis	16	21	28

REACH: test and cost reduction?



MODELS,

QSAR

Figure 6.1. Ecotoxicology is a multi-disciplinary study into the toxic effects of substances on species in complex systems [1].

REACH: implications

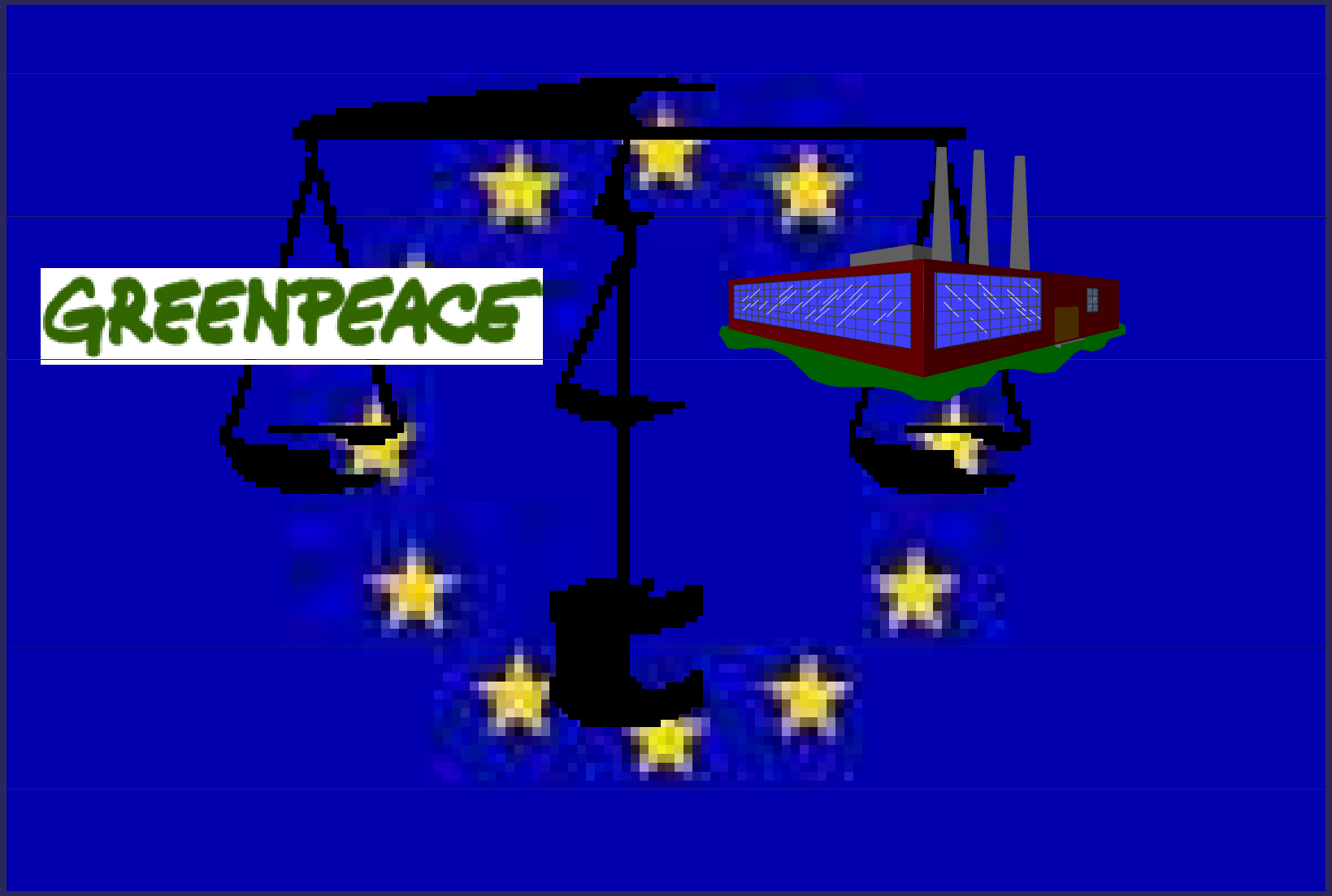
- Total: 2,8 to 5,6 billion €
- Industry pays
- Test costs(50-60% of total cost):
  - 86% for HH tests
  - 14% for environment tests
  - 0% for analyses
- Manpower and expertise?
  - Tests
  - Risk assessments
  - Evaluations

- Financial and time pressure: **danger for 'hazard-based' instead of 'risk-based' conclusions**

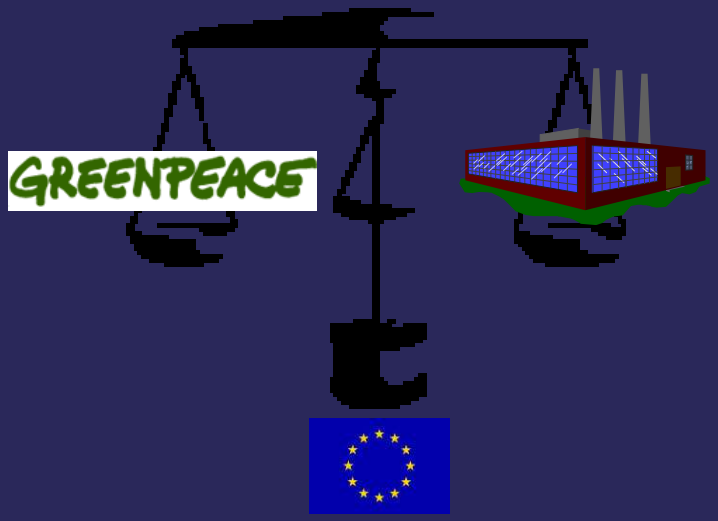
Závěrečné poznámky

Rizika toxických chemikálií

! rovnováha mezi vnímáním (ve společnosti), nejistotami, vědou, pragmatismem …



Případ chybějících …



… racionálních vědců

Dvě závěrečné poznámky

- Chemické látky kolem nás nebyly nikdy protestovány

… zejména neznáme ekotoxicitu
… ale pracuje se na tom

- Ekosystémy jsou složitější než si lidé myslí … ale pracujeme na tom

… předběžná opatrnost je na místě, nepředvídatelné dopady

Dr. Ludek Blaha
http://www.recetox.cz

blaha@recetox.muni.cz