

# Současná ekotoxikologie

## úvod

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FSS MU Brno, 23.9.2008

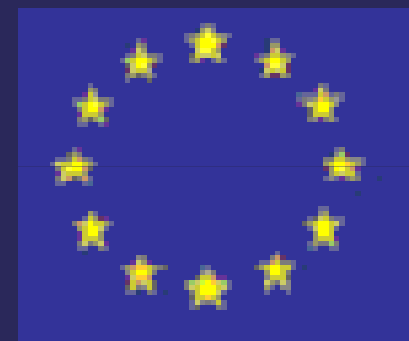


# WWW.RECETOX.CZ

= Výzkumné centrum pro chemii životního prostředí a ekotoxikologii



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



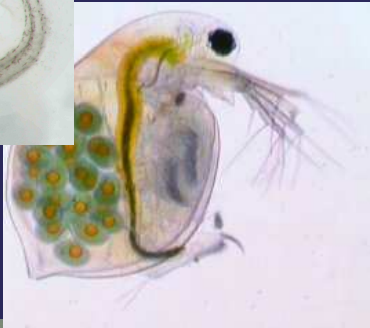
# RECETOX

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RECETOX





Ekotoxikologie

Chemie  
životního  
prostředí

Hodnocení  
vlivu na ŽP

**RECETOX**

Hodnocení  
ekologických a  
humánních  
rizik

Hodnocení  
environmentálních  
a biologických dat

Environmentální  
management a  
politika

- 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  
pollution  
ENVIRONMENTAL  
ENTERIC SCALE  
ENVIRONMENT  
ENVIRONMENT

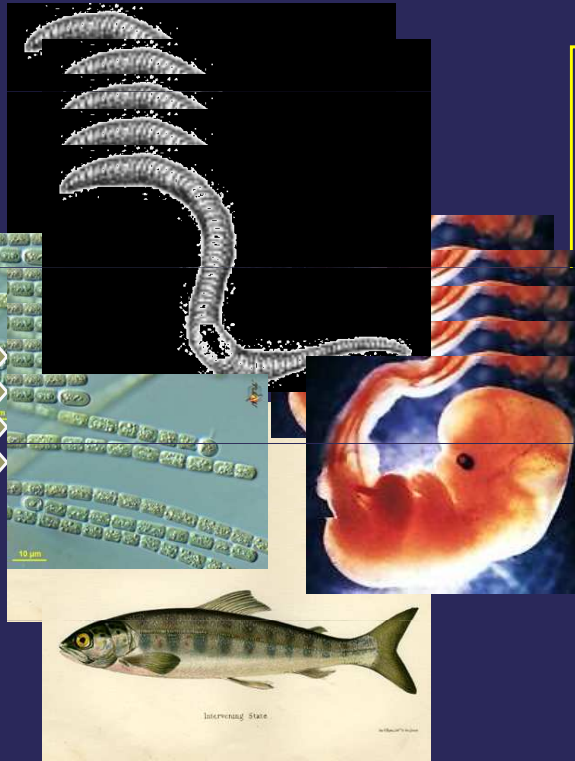
Hladiny znečištění  
LEVELS  
EMISSION SCALE  
ENVIRONMENTAL  
PROCESSES  
PROCESSES

Biodostupnost  
Bioavailable  
Bioavailable  
Bioavailable  
Bioavailable  
fraction  
fraction

"Expozice"

akutní

chronická



Chemikálie v  
CHEMICAL  
pollution  
ENVIRONMENTAL  
ENTERIC SCALE  
ENVIRONMENT  
ENVIRONMENT  
biomonitoring  
biomonitoring  
biomonitoring

Toxikokinetika  
Toxicokinetics  
Toxicokinetics  
Toxicokinetics  
Toxicokinetics

bioactive transformation,  
bioactive transformation,  
excretion, bioactive transformation,  
excretion, bioactive transformation,  
excretion, bioactive transformation,  
excretion, bioactive transformation,  
target site  
target site

"EFFECT"  
"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**

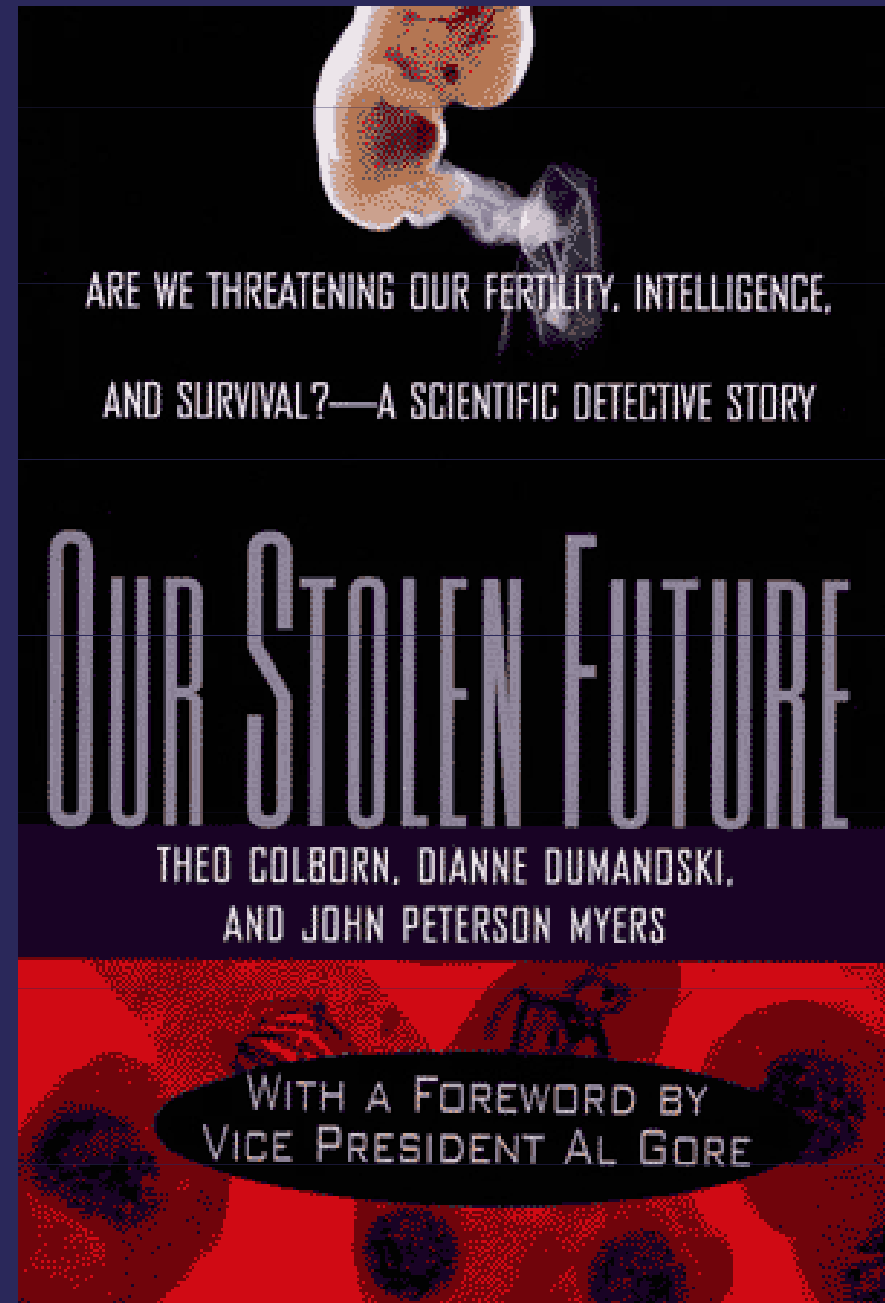
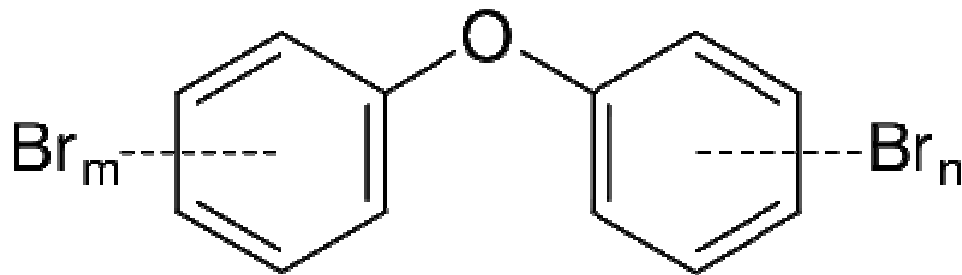
## Hlavní cíle ekotoxikologie

- **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 !

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



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.

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.

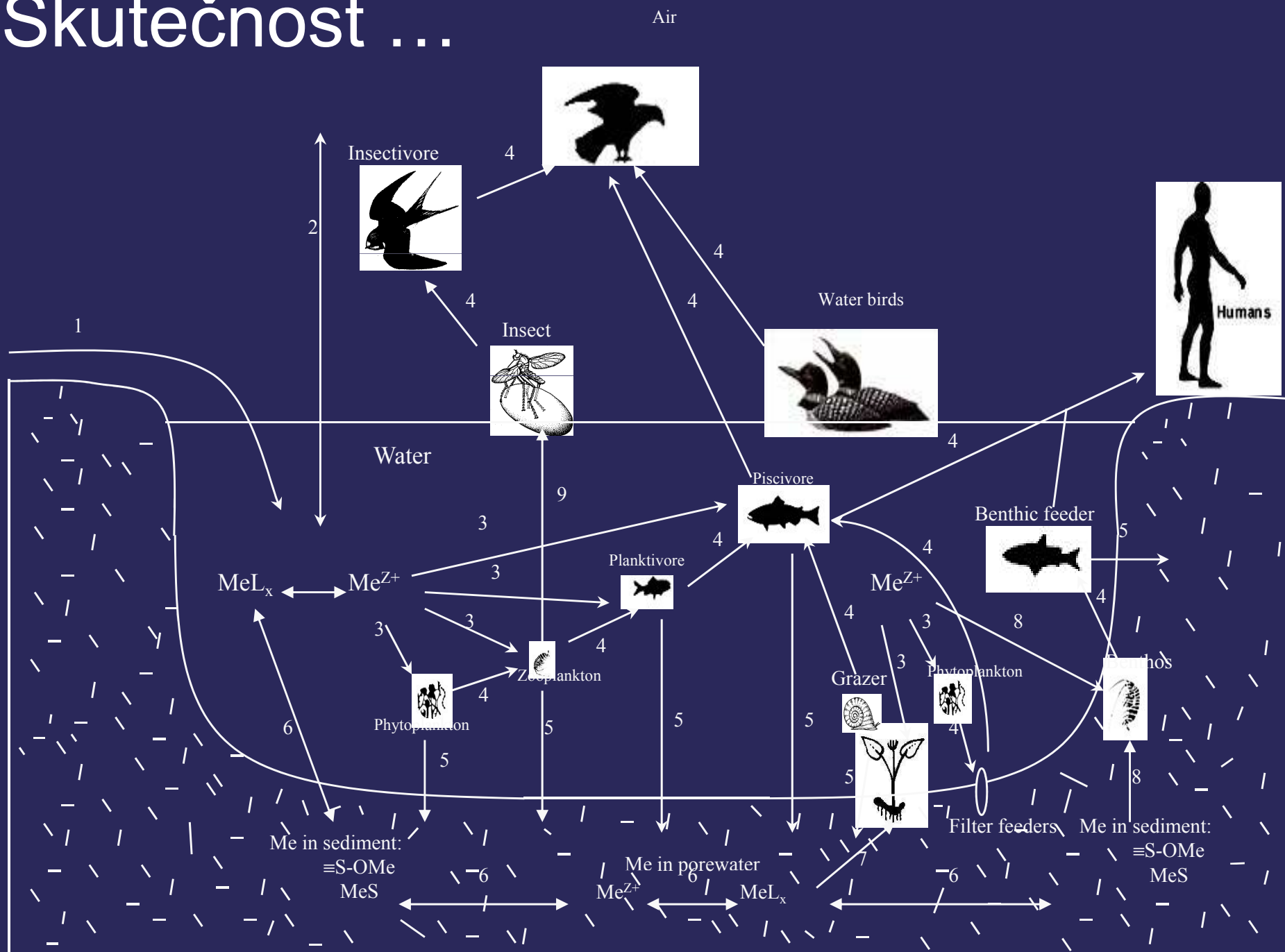
The team found that 48.3% of babies were female in the least polluted areas, but 49.3% were female in the dirtiest parts of town. After measuring the ratio of boys to girls born in all the areas, they calculated that 1,180 more babies would have been boys in the polluted areas if they had the same sex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



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

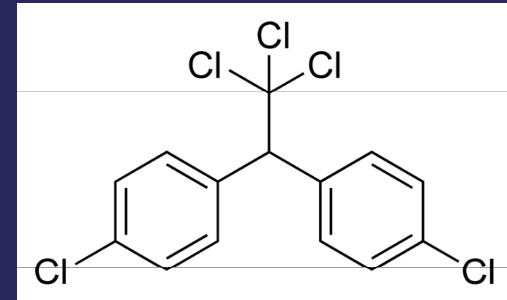
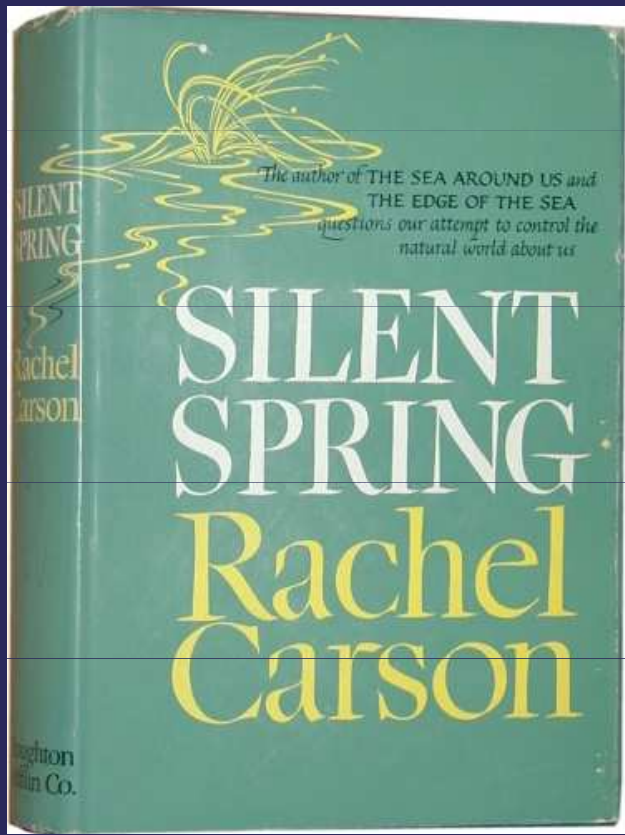
© Alamy

# Skutečnost ...



**Složitost (eko)systemu  
= složité problémy a komplikace ...**

1962



"DDT is good for me-e-e!"

The great expectations held for DDT have been realized. During 1946, exhaustive scientific tests have shown that, when properly used, DDT kills a host of destructive insect pests, and is a benefactor of all humanity.

Pennsalt produces DDT and its products in all standard forms and is now one of the country's largest producers of this amazing insecticide. Today, everyone can enjoy added comfort, health and safety through the insect-killing powers of Pennsalt DDT products . . . and DDT is only one of Pennsalt's many chemical products which benefit industry, farm and home.

**GOOD FOR STEERS**—Beef grows heavier nowadays . . . for it's a scientific fact that—compared to untreated cattle—beef steers gain up to 50 pounds extra when protected from horn flies and many other pests with DDT insecticides.

**GOOD FOR THE HOME**—helps **Knox-Out** to make healthier, more comfortable homes . . . protects your family from dangerous insect pests. Use **Knox-Out** DDT Powders and Sprays as directed . . . then watch the bugs "bite the dust"!

**GOOD FOR DAIRIES**—Up to 20% more milk . . . more butter . . . more cheese . . . tests prove greater milk production when dairy cows are protected from the annoyance of many insects with DDT insecticides like **Knox-Out** Stock and Barn Spray.

**GOOD FOR FRUITS**—Bigger apples, juicier fruits that are free from unsightly worms . . . all benefits resulting from DDT dusts and sprays.

**GOOD FOR ROW CROPS**—25 more barrels of potatoes per acre . . . actual DDT tests have shown crop increases like this! DDT dusts and sprays help truck farmers pass these gains along to you.

**KNOX FOR INDUSTRY**—Food processing plants, laundries, dry-cleaning plants, hotels . . . dozens of industries gain effective bug control, more pleasant work conditions with Pennsalt DDT products.

**PENN SALT CHEMICALS**

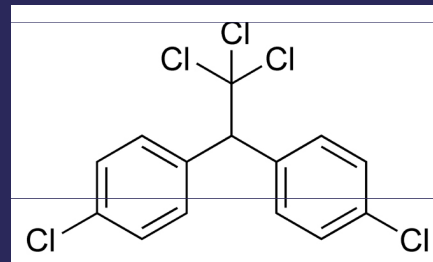
87 Years' Service to Industry • Farm • Home

PENNSYLVANIA SALT MANUFACTURING COMPANY  
WIDENER BUILDING, PHILADELPHIA 7, PA.

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



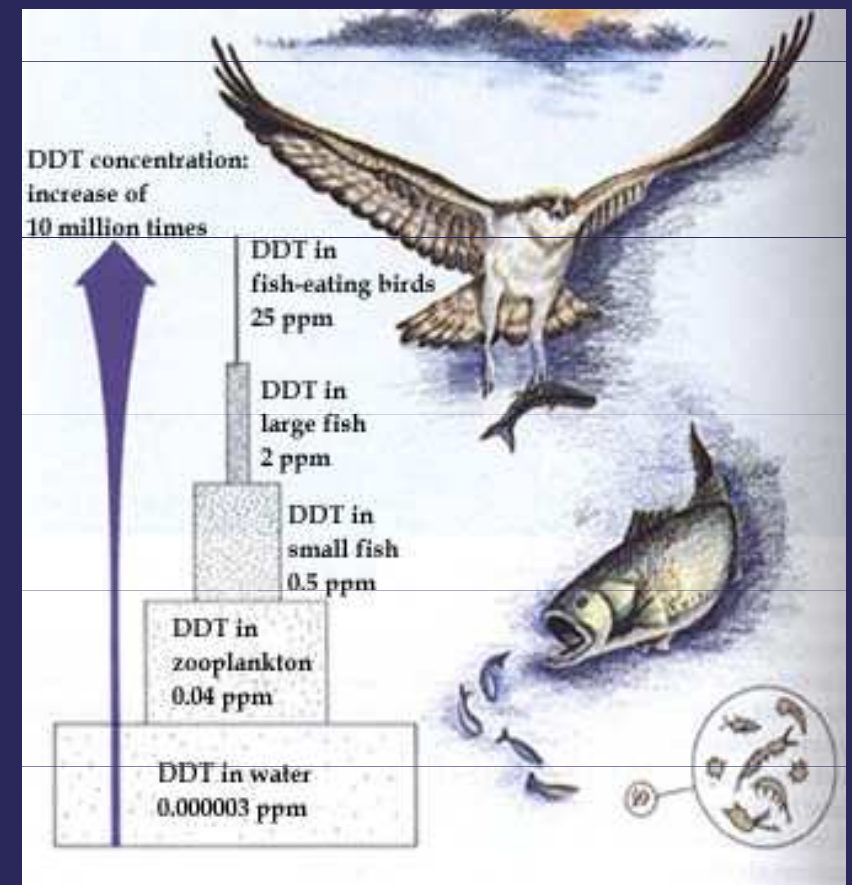
**Biochemie:**  
ptačí karbonátdehydratáza



**In vivo:** měknutí vajíček



**In situ:** bioakumulace  
-> úbytek populací ptáků



# Environmental (chemical) problems

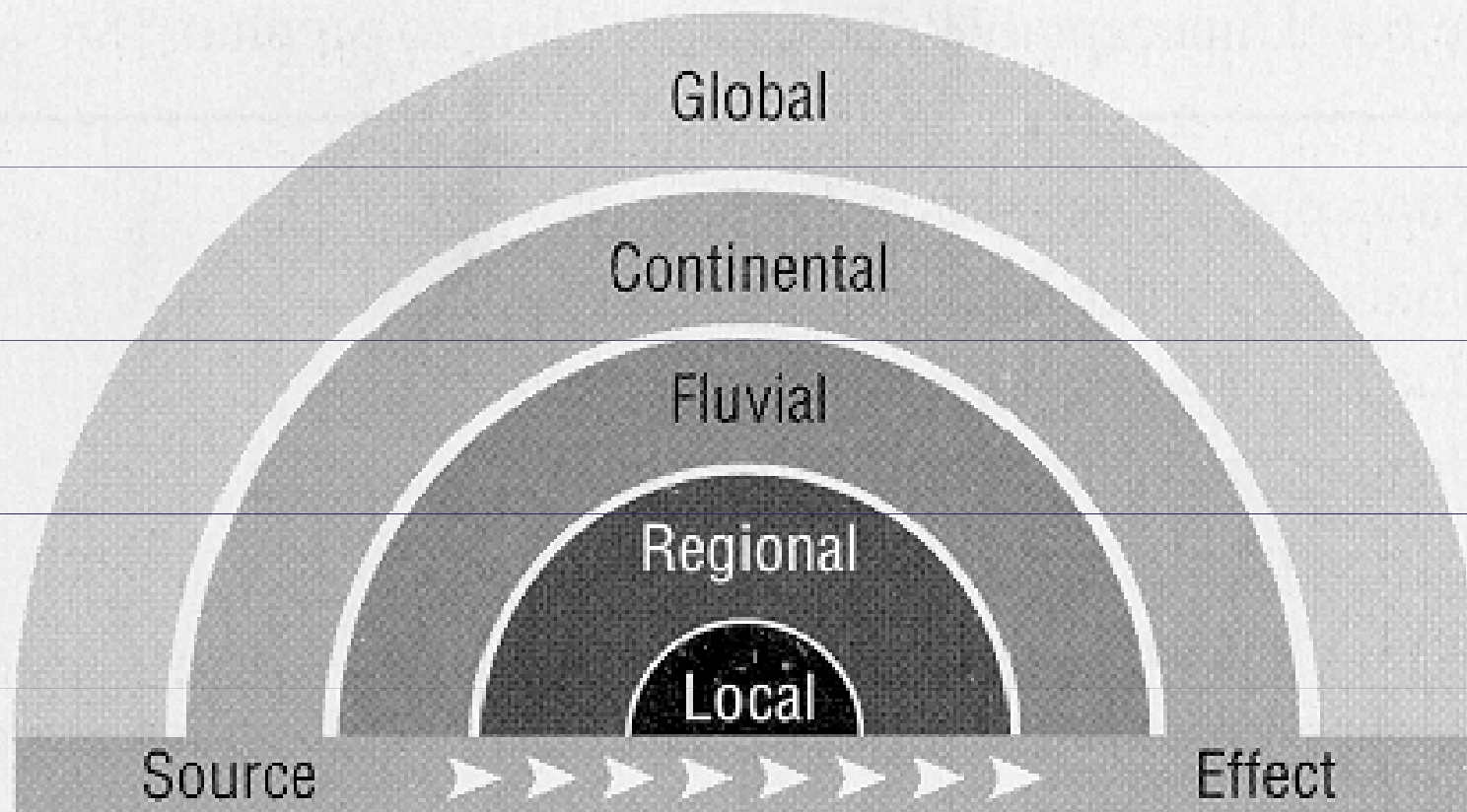


Figure 6.2. Five levels of scale at which environmental problems occur [9].



## 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.*

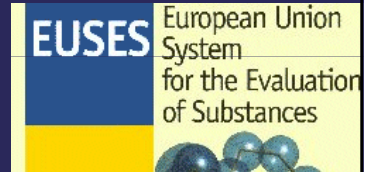
○ *Solely the dose determines that a thing is not a poison.*



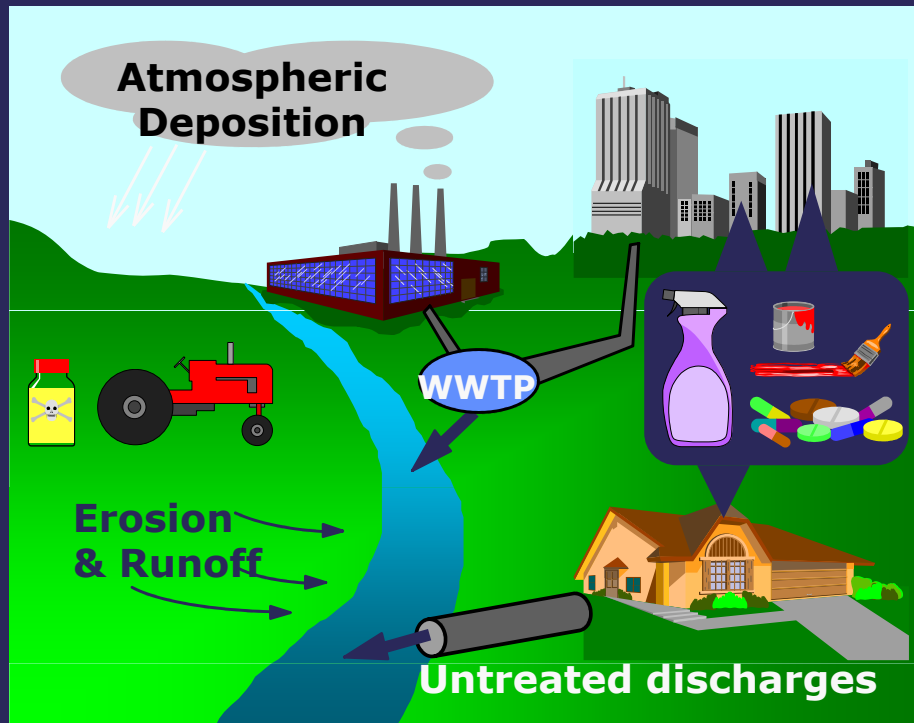


# Příčina -> Důsledek Dávka -> Účinek

-> Risk assessment = Hodnocení rizik

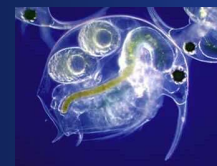


## Expozice (dávka)



## Efekt

(Jaká expozice vyvolá efekt ?)



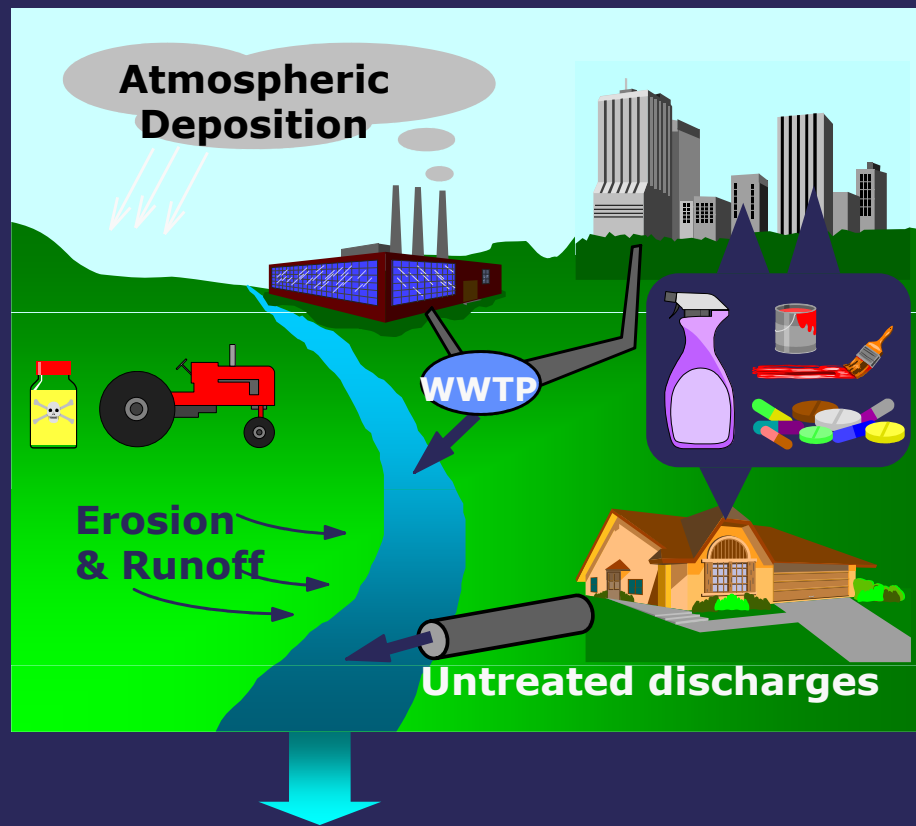
Laboratorní a polní studie  
Ekotoxikologické testy





# Jak poznat dávku (expozici) ?

## Expozice (dávka)



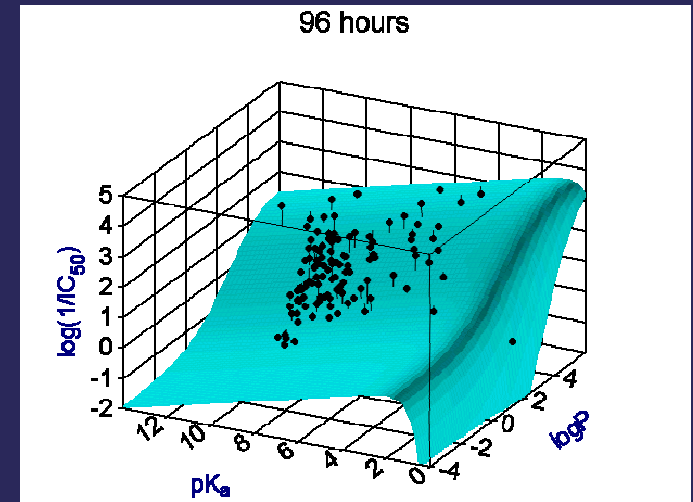
# Jak poznat, zda je látka „bezpečná“?

## PŘEDPOVĚDI

As, Hg ...

akutní toxicita pro ryby

$$\log(1/LC50) = 0.907 \cdot \log Kow - 4.94$$

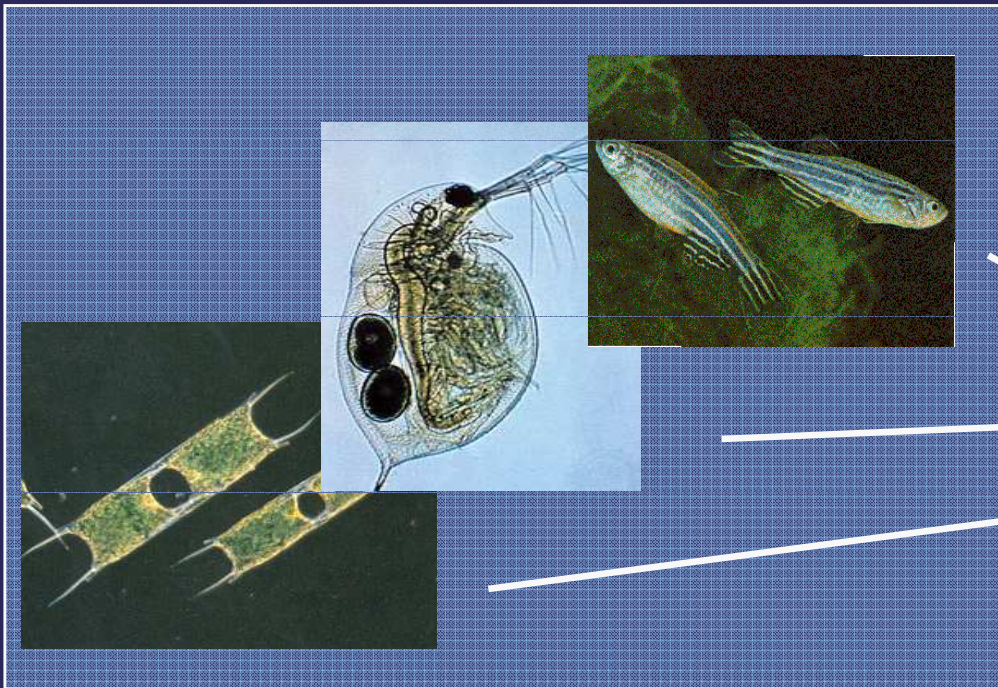


## TESTOVÁNÍ

- toxicita
- ekotoxicita



# Hodnocení účinků (ekotoxikologické testy)

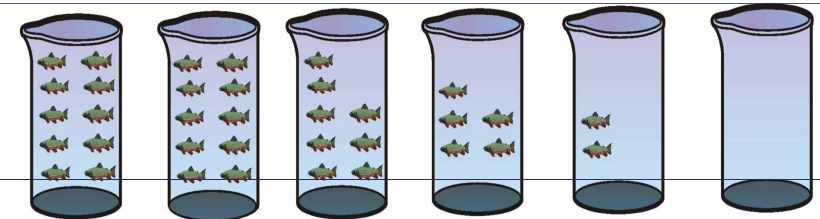


Cu addition



Concentration:

0.0  $\mu\text{g/L}$  13  $\mu\text{g/L}$  25  $\mu\text{g/L}$  50  $\mu\text{g/L}$  100  $\mu\text{g/L}$  200  $\mu\text{g/L}$



Control 1 2 3 4 5

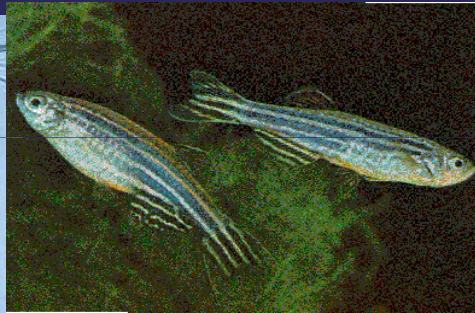
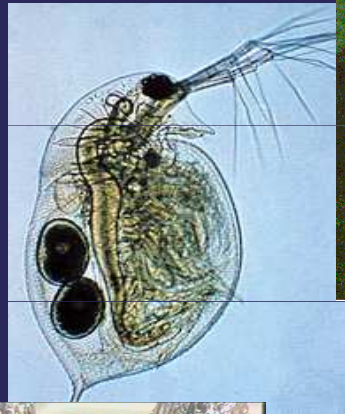
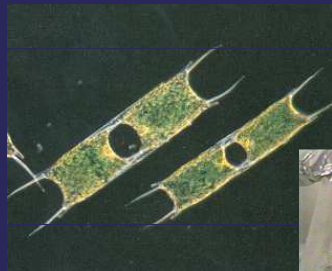
96-hour LC50 = 50  $\mu\text{g/L}$

Effect concentrations expressed in total/dissolved Cu



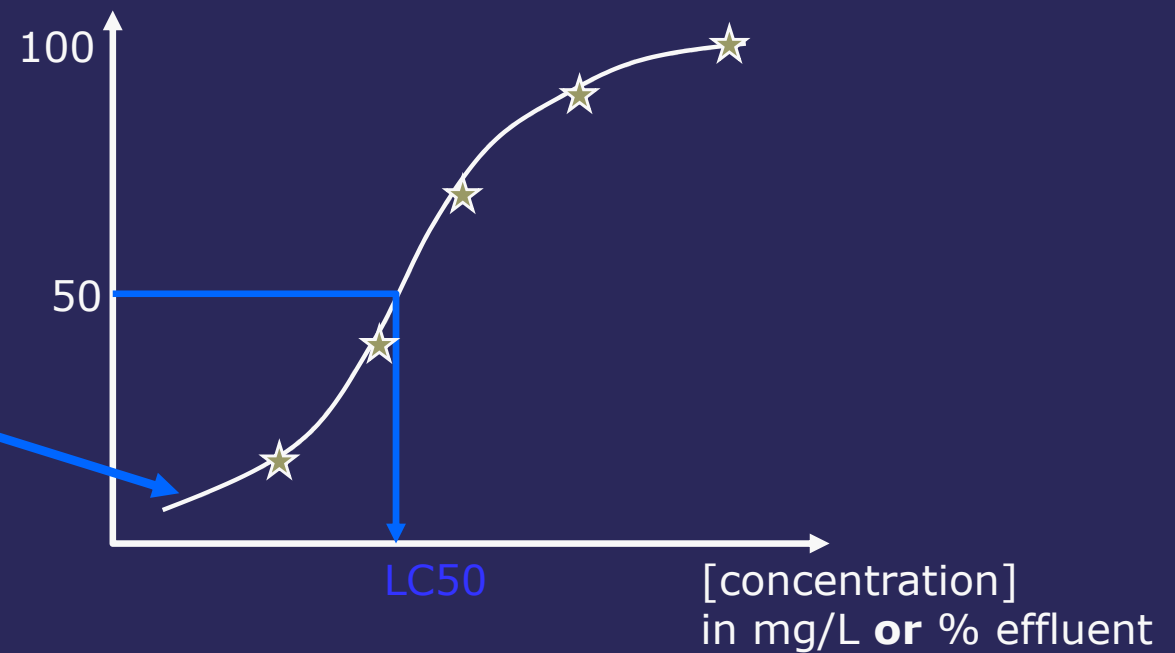
Extrapolation =  
PNECs or EQCs expressed in total / dissolved Cu

# Hodnocení účinků - výsledek



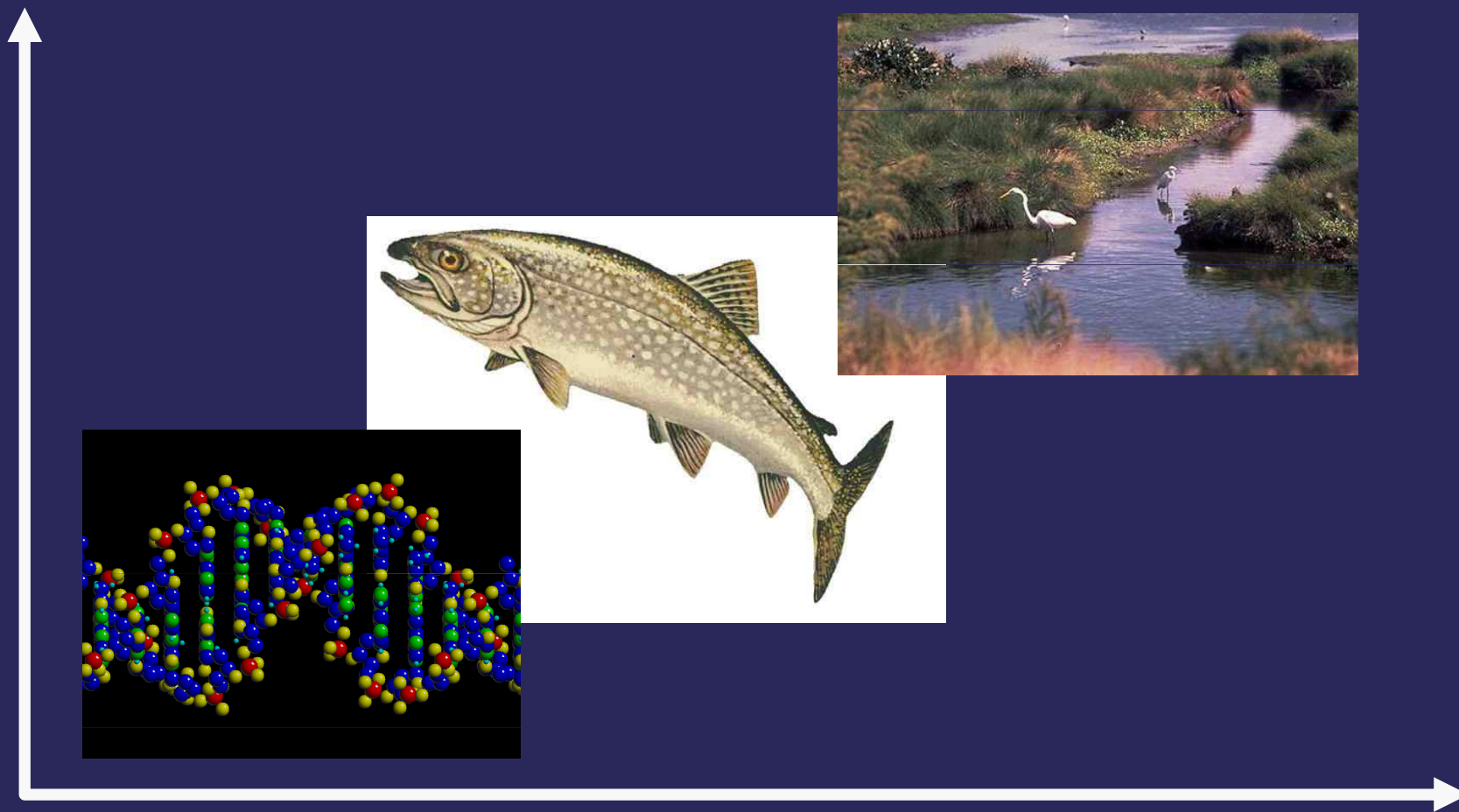
Threshold:

**No Observed Effect Concentration (NOEC)**



# Ekotoxikologické výsledky vs. realita (ekosystémy?)

1/přesnost (Nepřesnost)



Ekologická relevance



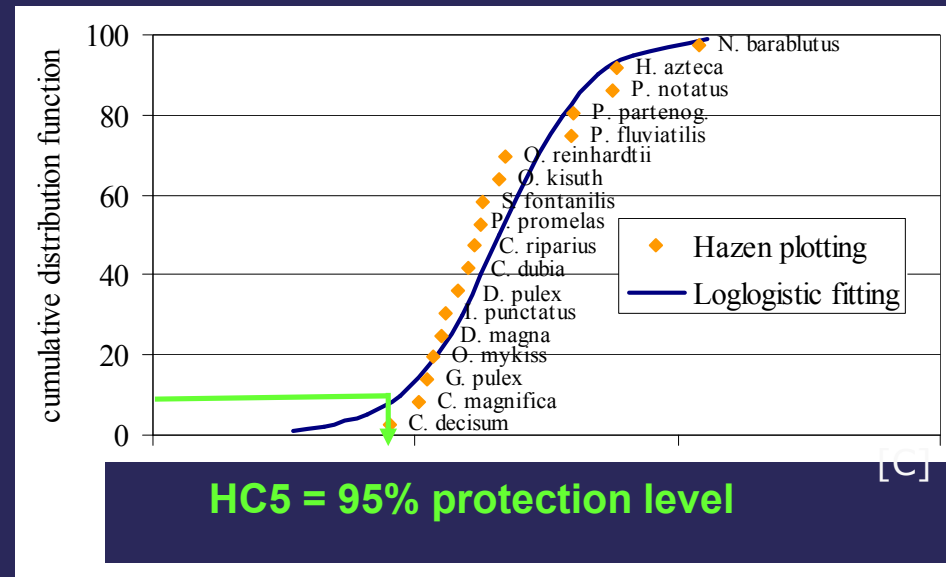
# Využití výsledků -> bezpečná dávka ?

Hodnoty ekotox. EC50

Extrapolace

Species sensitivity distribution (SSD)

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

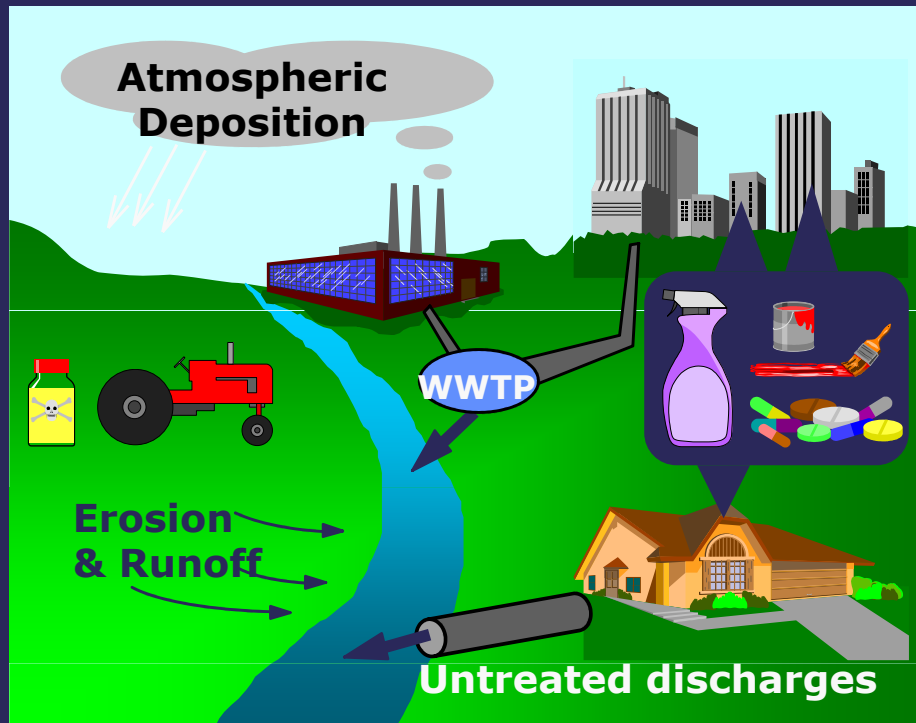


PNEC

# VYHODNOCENÍ RIZIKA

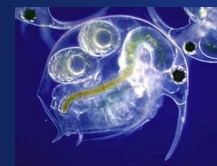


## Expozice (dávka)



## Efekt

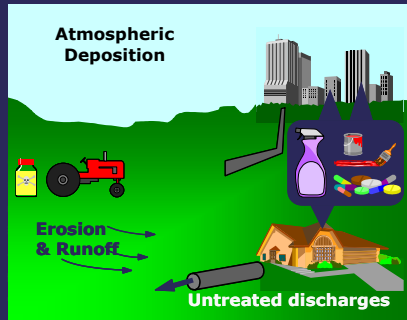
(Jaká expozice vyvolá efekt ?)



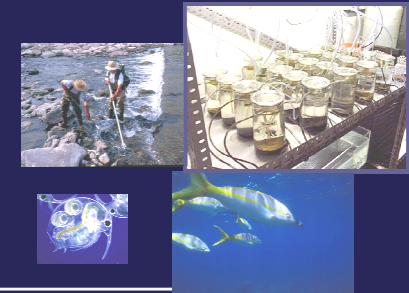
Laboratorní a polní studie  
Ekotoxikologické testy



# Charakterizace rizika

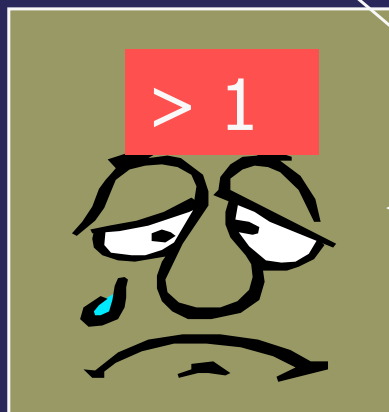


Definice nebezpečnosti

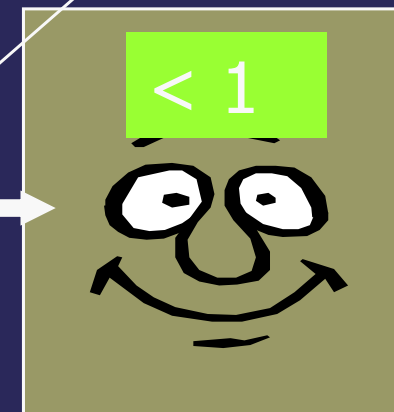


EXPOZICE  
PEC

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
<b>VII. Chlorované alifatické uhlovodíky</b>						
jednotlivě 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		
chllorethen (vinylchlorid)	0,1	10	20	20		
<b>VIII. Ostatní uhlovodíky (směsné, nehalogenované)</b>						
NEL	50	200	1000	50	50	200
<b>IX. Ostatní aromatické uhlovodíky (halogenované)</b>						
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			
<b>X. Ostatní</b>						
Anorganické látky						
B	100	500	5000		300	500
Cl <sup>-</sup>	25000	100000	150000	100000	150000	350000
F (F <sup>-</sup> pro vodu)	250	2000	4000	1500	1000	1500
NH <sub>4</sub> <sup>+</sup>	120	1200	2400	500	1000	3000
NO <sub>2</sub> <sup>-</sup>	25	200	400	100	100	200
S (sulfidická)	10	150	300		(d)	20
volně kyanidy/thiokyanáty	5	40	75			
komplex. kyanidy (pH<5)	10	250	500			
komplex. kyanidy (pH>5)	10	100	200			
Organické látky						
cyklohexanon	0,1	250	500			
fluláty (suma)	1	5	10			
hydrochinon	0,1	400	800			
pyrokatechin (katechol)	0,1	600	1200			
kresoly	0,1	100	200			
pvridin	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:

- Ověduší (! Lidé)
- Potraviný (! Lidé)
- Léky (! Lidé)
- Pitná voda (! Lidé)
- Orná půda (! Lidé)

## Matrice 2:

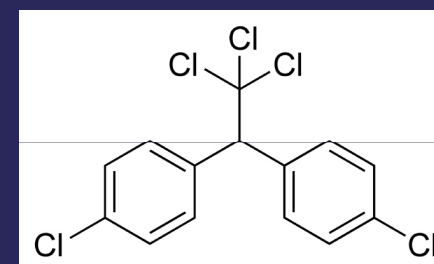
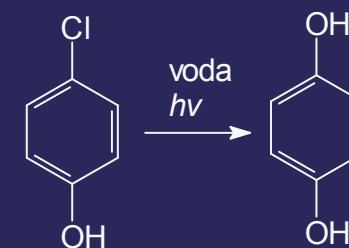
- povrchová voda
- odpadní vody
- pevný odpad

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

## Chemické látky:

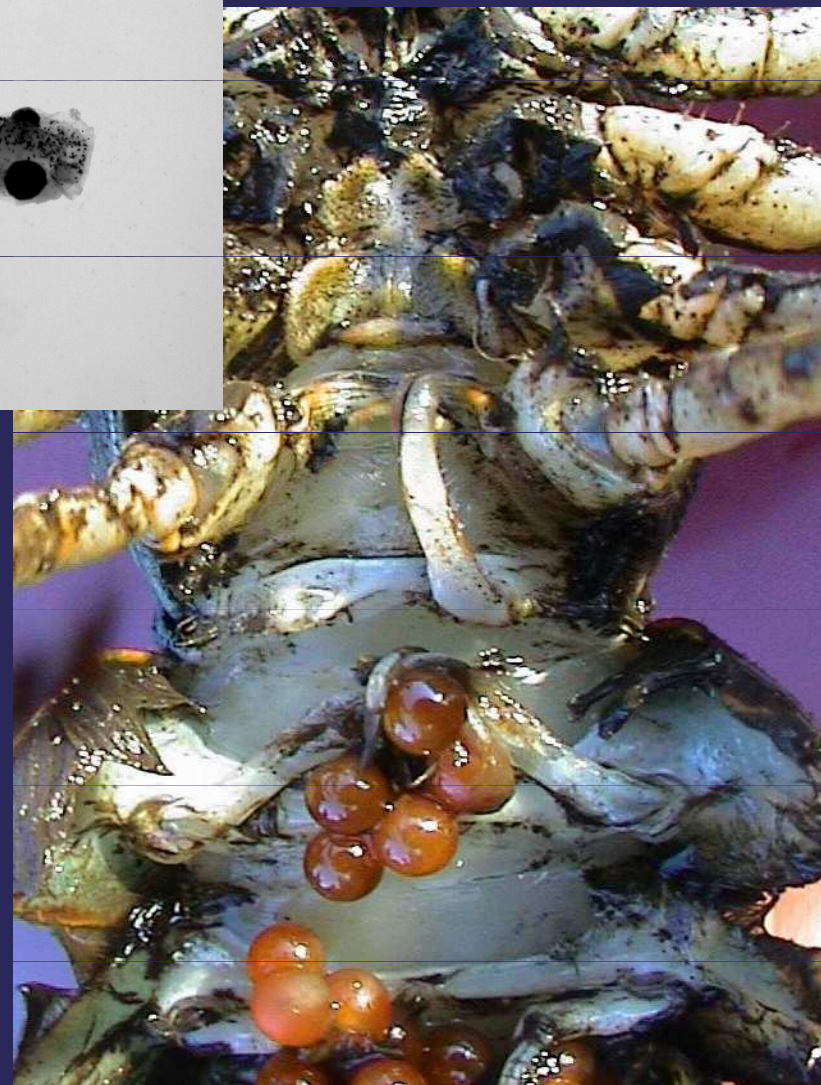
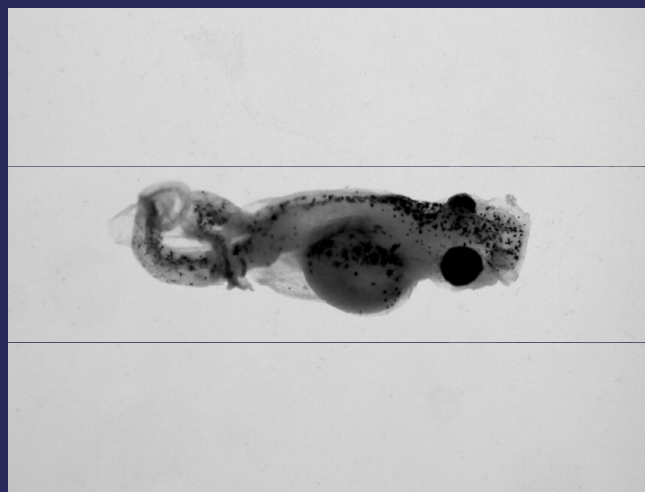
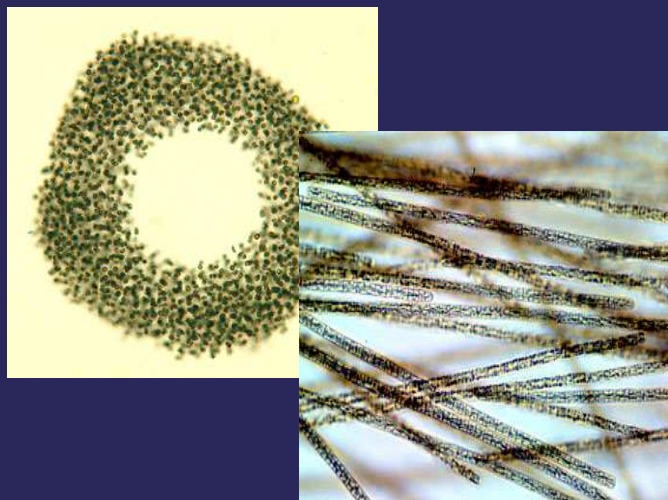
- PAHs
- chlorfenoly
- POPs
- tox. Kovy (As...)

*(formaldehyd ...*

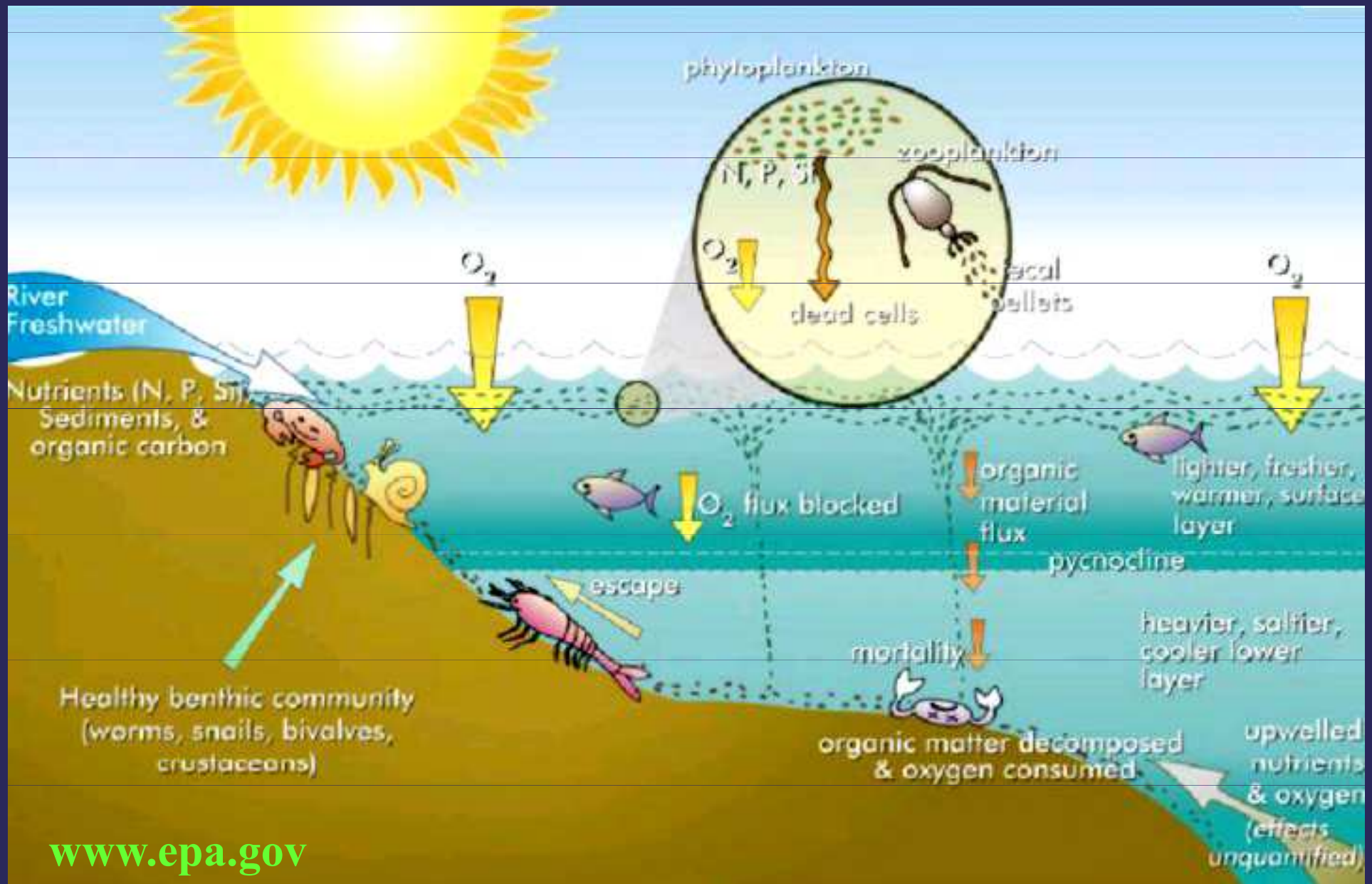


**Složitost (eko)systemu  
= složité problémy a komplikace ...**

# CHEMIKÁLIE V PŘÍRODĚ ... a organismy ... „toxicita není jen smrt“



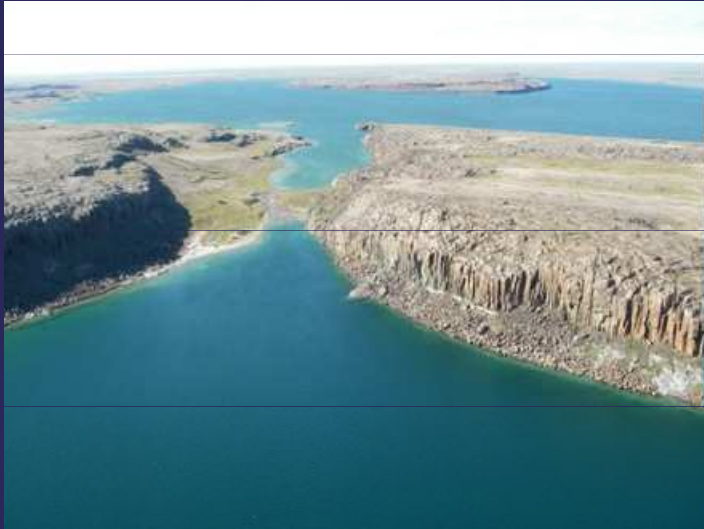
# Živiny ... jsou nebezpečné?



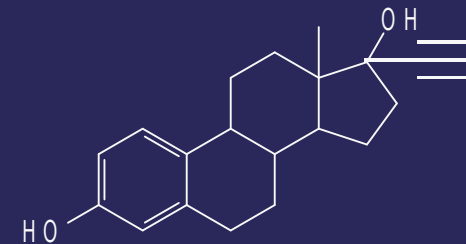




Kidd, K.A. et al. 2007. **Collapse of a fish population** following exposure to **a synthetic estrogen**. *Proceedings of the National Academy of Sciences* 104(21):8897-8901

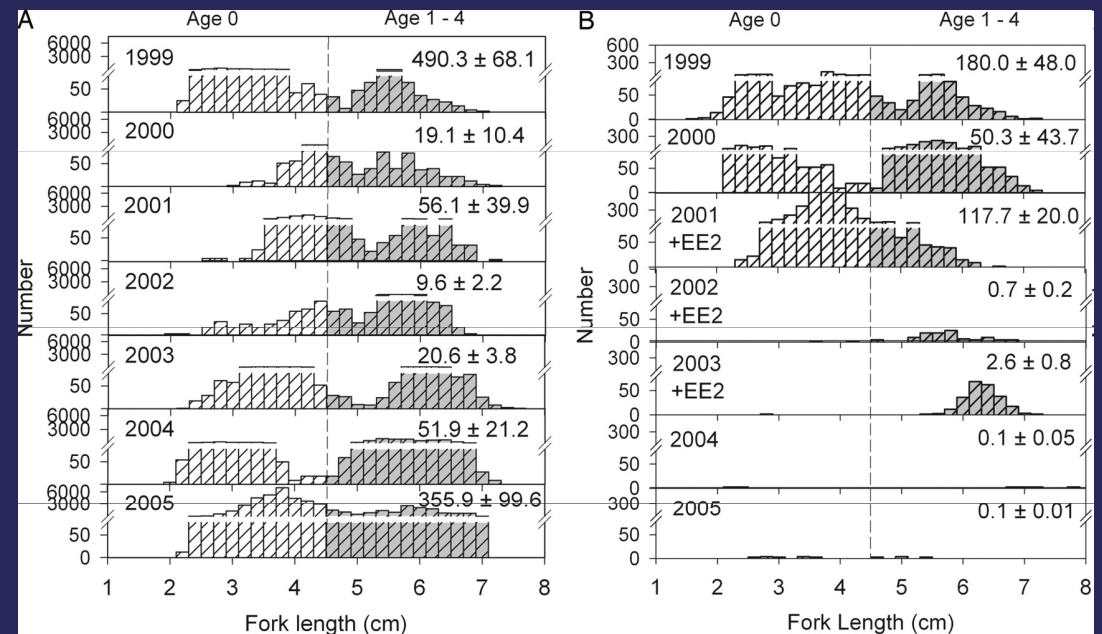
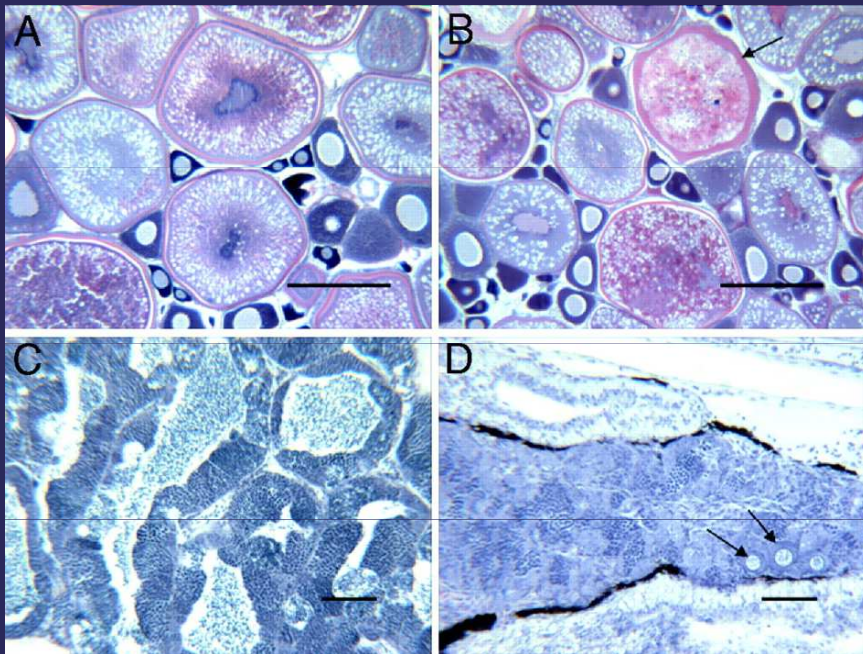


**5 ng/L (!)**  
**7 years**



**Controls**

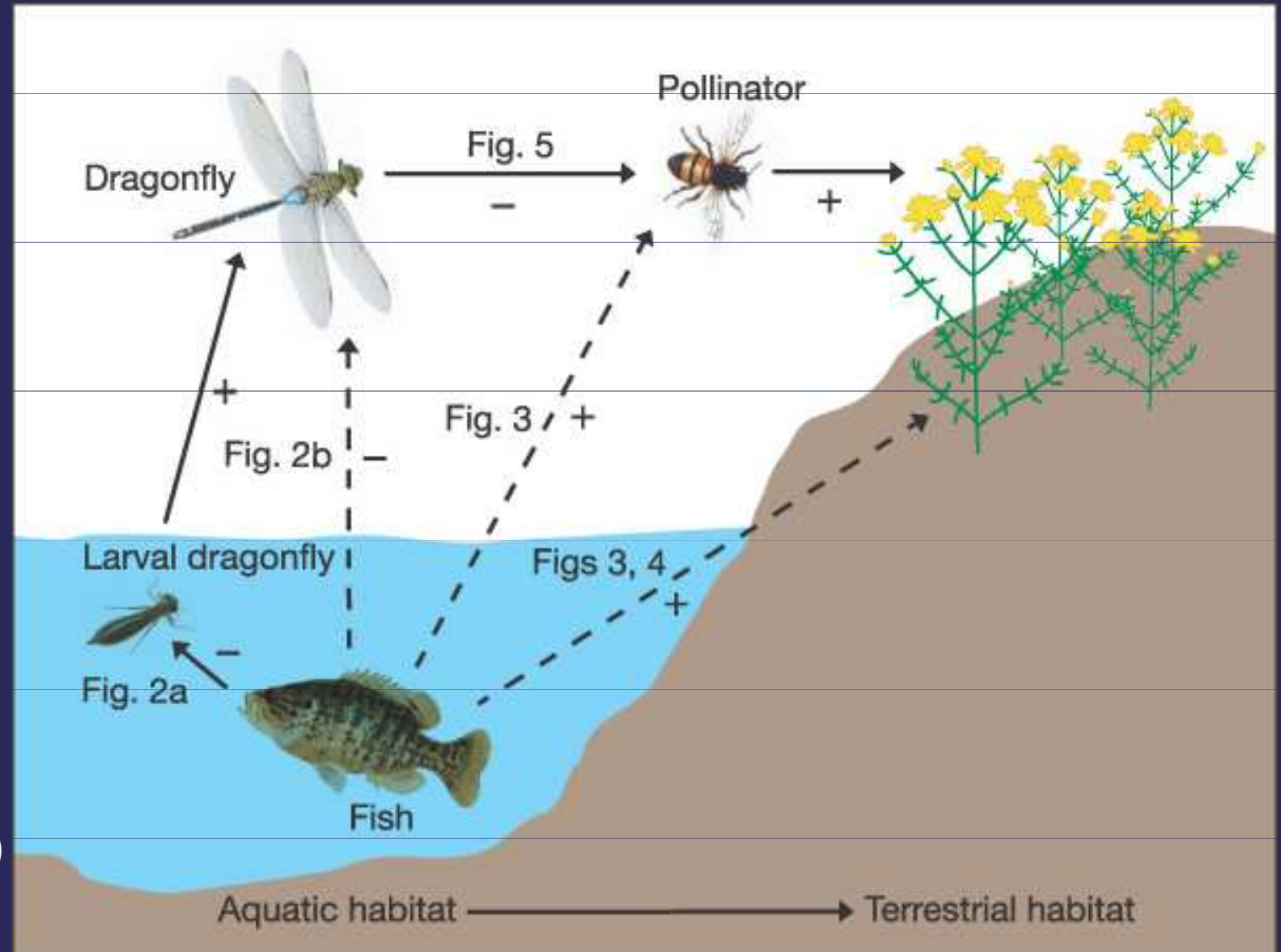
**+Ethinylestradiol**



- **ECOLOGY vs ECOTOXICOLOGY**

- Key / Keystone species

- dramatic changes in all community – example: FISH !

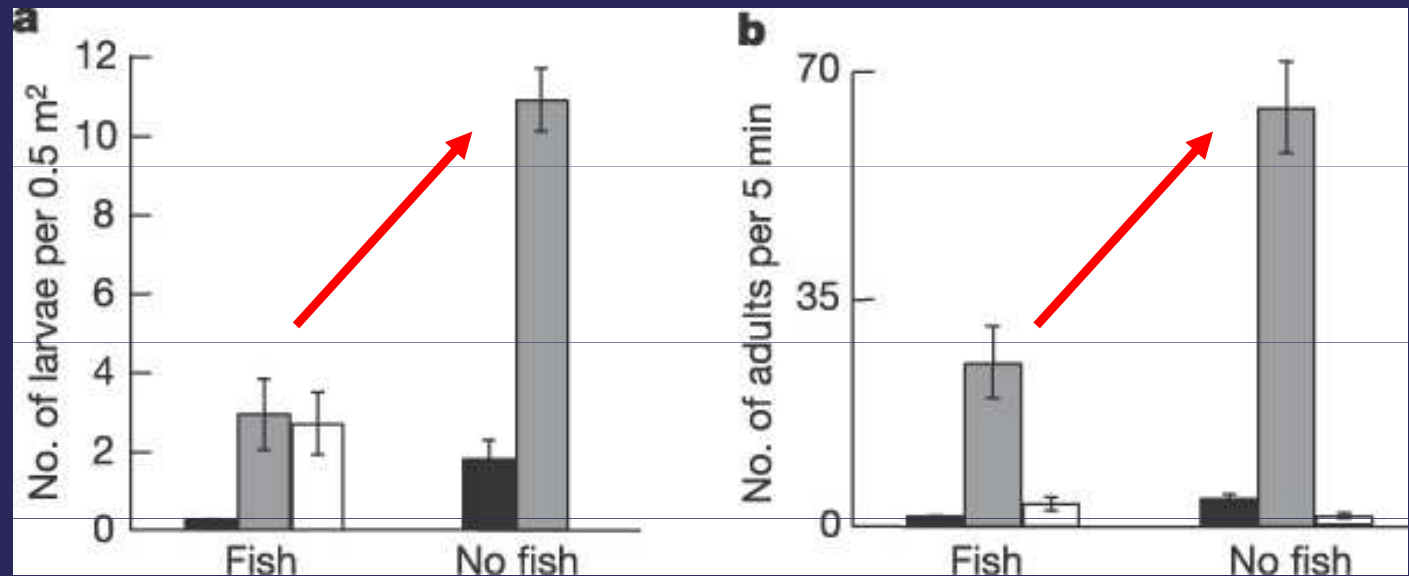


**Knight et al.,  
NATURE (2005)  
437: 880**

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

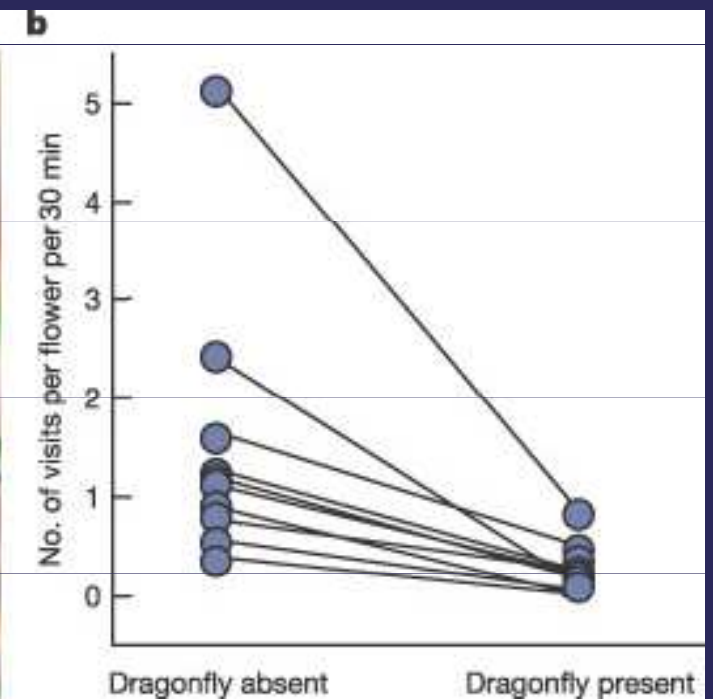
## No. of dragonflies

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

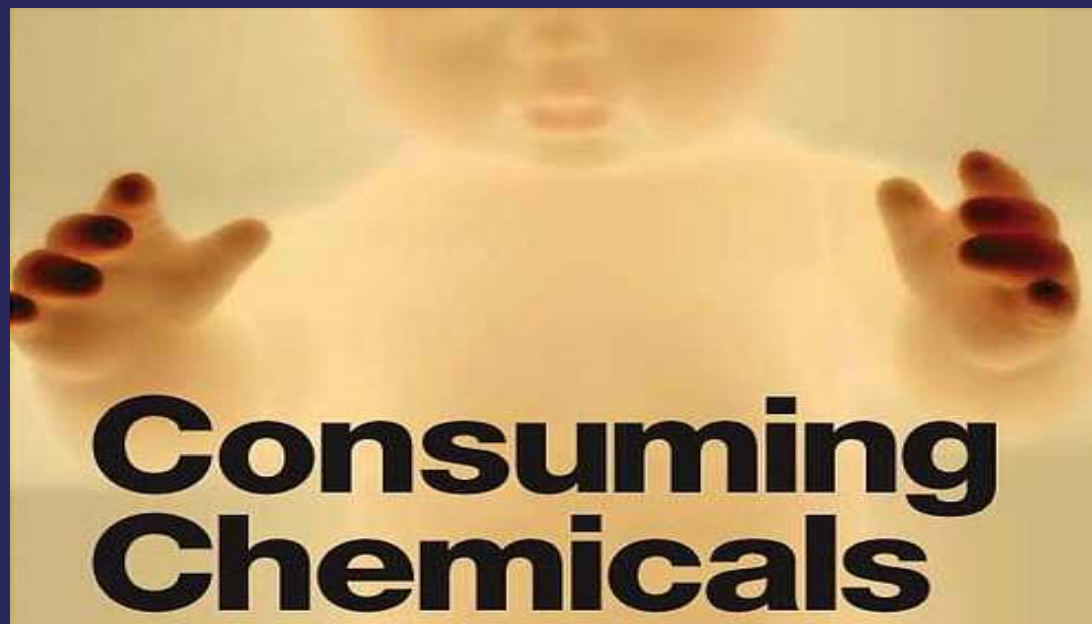
- 100196 substances in EINECS
- 2747 HPVCS (Allanou et al., 1999)
  - 14% minimum data-set (base-set)
  - 65% less than base-set
  - 21% no toxicity data
- Priority lists
- Situation in 2005 (after 10 years )
  - 141 substances RA status
  - 74 draft RAR
  - **48 final RAR**

# 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

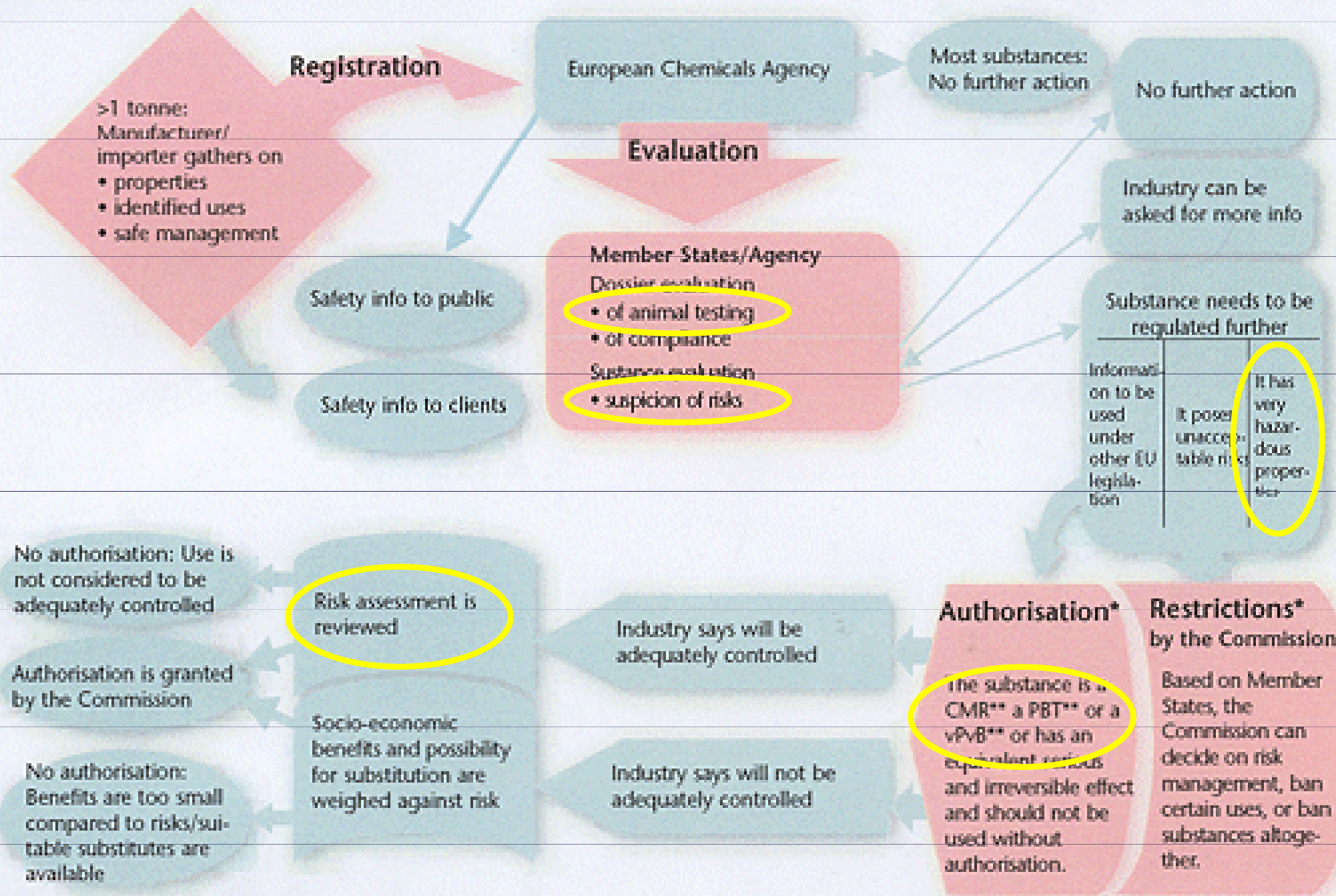


## Registration, Evaluation and Authorisation of Chemicals

- 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](http://echa.europa.eu))



\* 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 competitiveness 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, carcinogenicity,...
- 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. <i>in vivo</i> )	5923 (20.1)	6910 (23.5)	8182 (27.9)
6.4.4 <i>In vivo</i> 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 <i>Daphnia</i> toxicity	2321 (7.9)	4096 (14.0)	8798 (30.0)
6.1 Skin irritation/corrosion (incl. <i>in vivo</i> )	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	<b>Toxicological information</b>	<b>Ecotoxicological information</b>
1-10 t/y	<b>14</b>	<b>4</b>	<b>1</b>
10-100 t/y	<b>14</b>	<b>14</b>	<b>7</b>
100-1000 t/y	<b>17</b>	<b>19</b>	<b>18</b>
> 1000 t/y (HPVs ~ 2747)	<b>17</b>	<b>22</b>	<b>25</b>





# 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 <i>In vivo</i> 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**

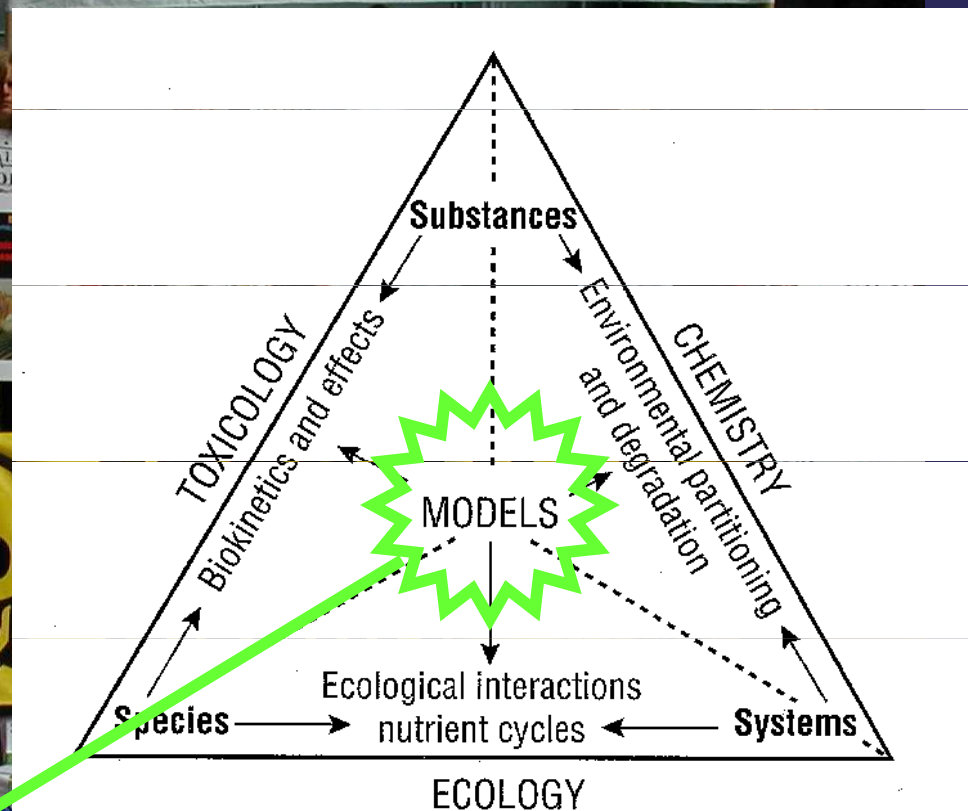


Figure 6.1. Ecotoxicology is a multi-disciplinary study into the toxic effects of substances on species in complex systems [1].



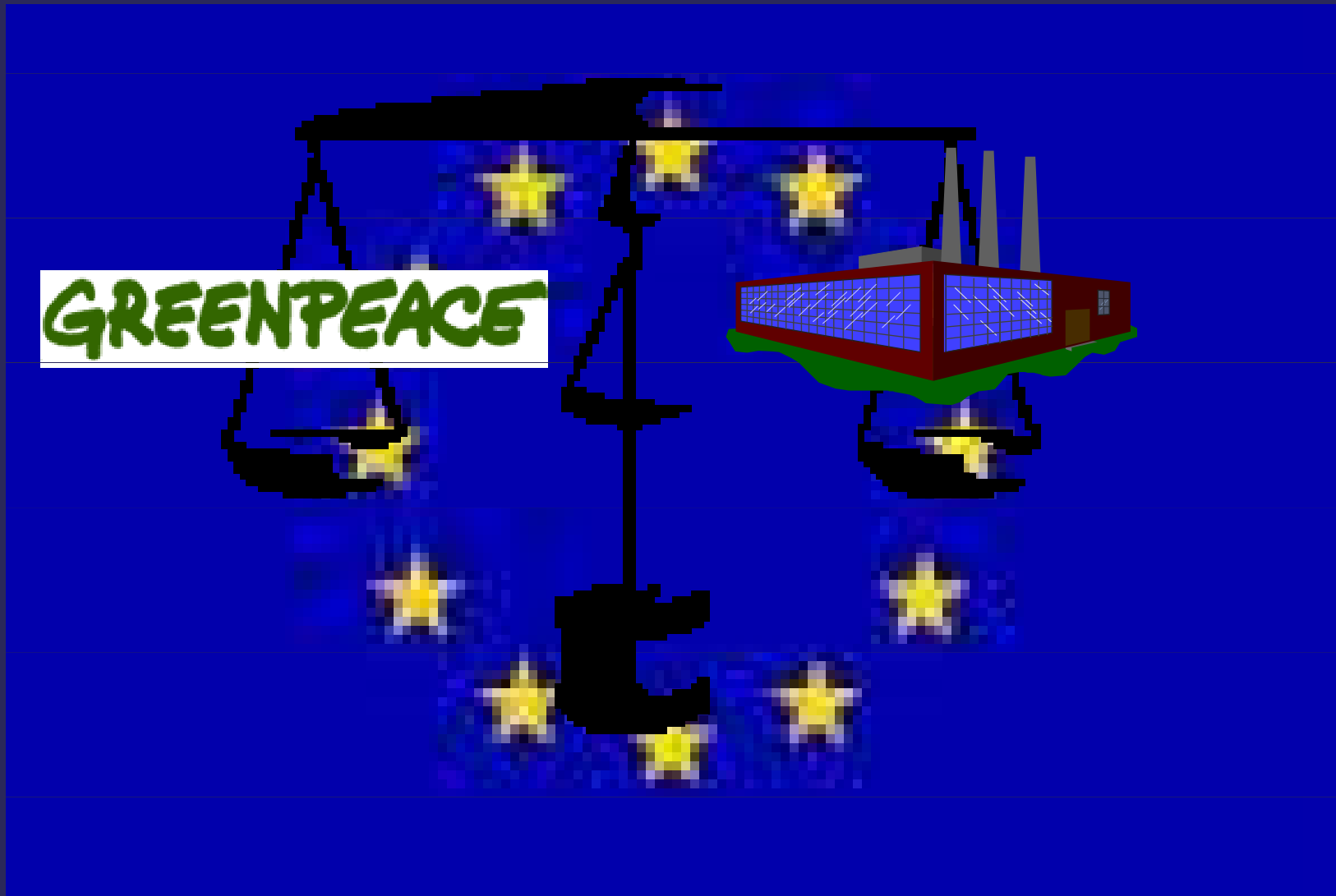
# REACH: implications

- 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*



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