

Workshop „Micropollutants, metabolites and mixtures in drinking water and its sources“, 18.06.2012
in Nieuwegein

**Toxicity assessment
(methods, parameters, endpoints,
evaluation of results)**

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Umwelt
Bundes
Amt
für den
Bundesrat

Workshop on micropollutants, metabolites and mixtures
June 18 2012, Nieuwegein (Netherlands)

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Theoretical concept

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    graph LR
      A[Product development] --> B[High dose mechanisms]
      B --> C[Toxicological Risk]
      D[Environment] --> E[Low dose range]
      E --> F[Toxicological Safety]
  
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Basic consens

Benefit-risk balance

Strategies for prevention and control

- State-of-the-art: Adequate monitoring and regulation

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Evaluation of partly or non-assessable substances in drinking water (1)

Recommendation of the German Federal Environmental Agency
after consultation with the Drinking Water Commission of the
Federal Ministry of Health
2003

"Evaluation from the point of view of health of the presence in
drinking water of substances that are not (yet) possible or only
partially possible to evaluate"

<http://www.umwelt.daten.de/wasser-e/empfnichtbewertstoffe-english.pdf>

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Evaluation of partly or non-assessable substances in drinking water (2)

To assess the presence of substances in DW in cases in which

- Data that would allow an assessment of the human toxicology is non-existent or incomplete, and
- Their possible presence in DW is not regulated by a limit value (but only by the requirement of the DW Ordinance: *Drinking water may not contain chemical substances in concentrations that are liable to damage human health*),

UBA and DW Commission recommended a pragmatic health-based parametric value (HPV) (maximum permitted concentration) of

HPV = 0.1 µg/l

as the initial basis for evaluation.

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Evaluation of partly or non-assessable substances in drinking water (3)

The HPV is a **precautionary value** for substances easily expanding into drinking water, for which an evaluation on the basis of human toxicology is not possible, or only partially possible.

Its level is calculated in such a way that a subsequent, complete evaluation of the human toxicology of a non-genotoxic substance (with an effect threshold) or of a genotoxic substances (without an effect threshold) will with certainty produce an equivalent or higher guide value for lifelong consumption that is tolerable or acceptable in terms of health.

Evaluation of partly or non-assessable substances in drinking water (4)

For those substances possibly present in DW with increasing density of data the following maximum (safe) *values for health for lifelong consumption* in DW can be expected:

- ≤ 0.1 µg/l: there are only inadequate or no toxicological data at all available, the substance is genotoxic or is suspected to be **genotoxic**;
- ≤ 0.3 µg/l: the substance has been proven to be **non-genotoxic**, but otherwise there are no significant experimental toxicological data available;
- ≤ 1 µg/l: the substance has been proven to be **non-genotoxic** (see above). In addition, there are significant *in vitro* and *in vivo* data on the **oral neurotoxicity** of the contaminant. However, these data do not produce a value lower than 0.3 µg/l;
- ≤ 3 µg/l: the substance is neither genotoxic, nor neurotoxic (see above). In addition, there are significant *in vivo* data from at least one study on subchronic-oral toxicity of the contaminant. However, these data do not produce a value lower than 1 µg/l.

Evaluation of partly or non-assessable substances in drinking water: A health based approach

Genotoxic + substance metabolically relevant in humans?	YES	NO	NO	NO	NO	NO
Genotoxic?		YES	NO	NO	NO	NO
Immuno- and/or Neurotoxic?			no data	NO	NO	NO
Subchronic toxicity?				no data	NO	NO
Chronic toxicity?					no data	NO
Chronic toxicity?						NO

Why conduct Bioassays?

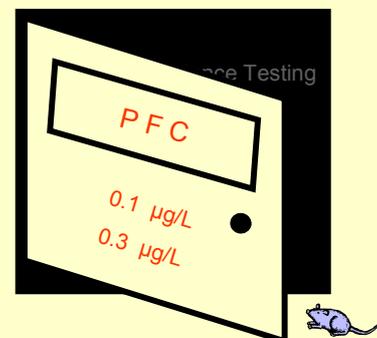
- Because we can
- A mismatch in the awareness of possible toxicological effects is causing erosion in public acceptance of (expensive) environmental management actions
- Precautionary anticipation of novel environmental hazards
- There is therefore, a priority requirement to implement the use of robust but simple, easy to learn, cost-effective test systems, which can be linked to adverse effects.

Precautionary Principle

For drinking water quality the precautionary principle is especially justified, because as a basic food, consumers have no choice of consumption. Once spoilt, it could at best be treated afterwards but could not be recalled or replaced. Also, water is consumed by an especially large number of potential high-risk groups in considerably higher daily quantities (2 kg and more) than other foodstuffs. In addition, if highly populated areas were to be excluded from central drinking water supply in account of health risks, water-borne sewer systems would break down quickly. Thus, considerably high risks for epidemics would be an inevitable result.

In order not to ever „risk“ such an scenario, quality of all waters for human use must satisfy the strictest precautionary principles. An individually adapted, strictly hazard-related risk management in the form of „post-treatment“ should only be needed for individual cases or accidents.

At the door - the value ...



Behind the door - the way ...

Substance Testing

- Mode of Action
- Exposure Information

0.1 µg/L
0.3 µg/L

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Measured data

Compounds	Detected maximum concentrations (ng/L) *	
	Surface water	Drinking water
Perfluorocarboxylic acids		
Perfluoropentanoic acid	1638	77
Perfluorohexanoic acid	1248	56
Perfluorooctanoic acid	3640	519
Perfluorodecanoic acid	Not specified	Not specified
Perfluorosulfonic acids		
Perfluorobutane sulfonate, Potassium salt	71	26
Perfluorooctane sulfonate, Potassium salt	193	22

* Reference: Skutlarek et al; Environ Sci Pollut Res 13(2006):299-307

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PFC - Test strategy and methods in genotoxicity testing

In vitro short-term tests

Bacterial assay
Ames I

Cytotoxicity
Plating

Micronuclei

FACS

ISO - Standard

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PFC - Summary Assessment

- 1 Minimal Dataset Cytotoxicity/Genotoxicity
- 2 Mode of Action (MOA)
 - Cytotoxicity
 - Influence on the Cell Proliferation
- 3 No Evidence for a genotoxic effect mechanism as the cause for appearance of liver tumors in laboratory animals

↓

German Drinking Water Commission :

(Lifelong, health based) Precautionary Action Value, e.g. in case additional perfluorocarbons would be present
 $PV = 0.1 \mu\text{g/l}$ (for Σ PFOA + PFOS)

(Strictly health based) Guide value
 $GV = 0.3 \mu\text{g/l}$ (for Σ PFOA + PFOS)

(Still) Tolerable for safe lifelong exposure of all population groups!

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Axiom of concern

According the seventh article „Water“ of the German Protection Against Infection Act (Infektionsschutzgesetz, IfSG), § 37 of which is amongst others the basis of the German Drinking Water Ordinance of 2001 (TrinkwV 2001), „water for human use (...) must be of such quality that there is no reason to fear any damage to human health, particularly through pathogens, being involved in its consumption or use“.

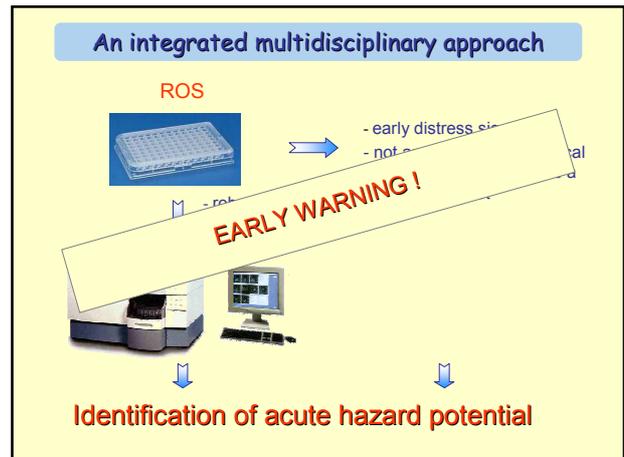
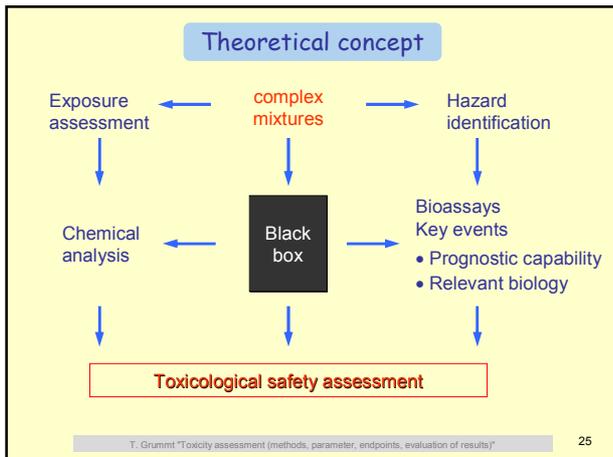
The statement „free of concern“, legalized in the IfSG, expresses a quality requirement, with demands not only the prevention of scientifically quantifiable and accordingly known risk potentials, but also precautionary measures against those risk potentials which can be exoected on the basis of plausible risk assessments and appear to be greater than zero although they cannot be quantified (yet).

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Axiom of concern (continued)

Thus this so-called *axiom of concern* (*Besorgnisgrundsatz*) requires a drinking water, the quality and purity of which is higher than could be described toxicologically by single substance analysis for life-long consumption. This requirement for example must also be satisfied by a drinking water which contains substance mixtures or substances for instance from oxidative treatment steps which cannot be assessed completely (yet) in regard to toxicology.

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Risikomanagement von neuen Schadstoffen und Krankheitserregern im Wasserkreislauf

T_{OX}BOX

<http://www.riskwa.de/>

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Thank you for your attention !