FEDERAL INSTITUTE FOR RISK ASSESSMENT

BfR
Bundesinstitut für Risikobewertung

Expert Meeting to Reach Scientific Consensus on Endocrine Disruptors

Goals and Perspective of the Meeting

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Picture sources: BfR; UNEP

One Substance – One Toxicological Assessment?

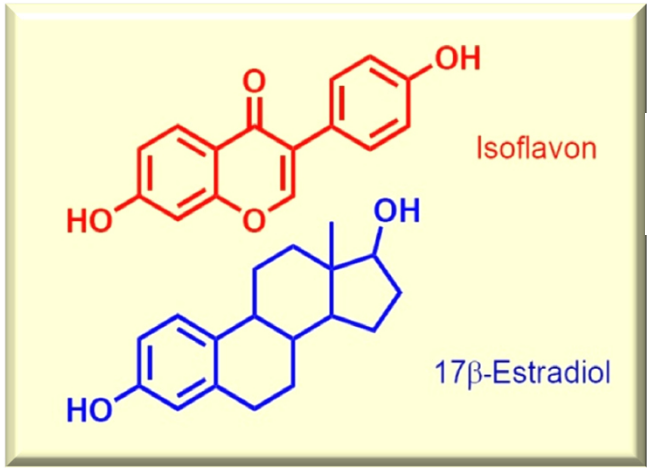
Real world: - different regulations
- different data requirements (from all *in vivo* to *in vitro* only)
- different regulatory consequences (from ban to not yet regulated)

Plant Protection Products (EC1107/2009) / Biocides (EU 528/2012)	Pharmaceuticals	Food additives (EC 1333/2008)	REACH (EC 1907/2006)	Plastics with food contact (EU 10/2011)	Cosmetics (EC 1223/2009)	Food and others
Are data requested under the regulation sufficient for identification?						
✓	✓	✓	(✓) depending on production volume	(✓) depending on migration from material	(✓) depending on intended use	👎 usually no product specific tox data
What are the principle(s) of regulation?						
Approval procedure	Approval procedure	Approval (EU lists of approved additives: AII/III)	Registration, authorisation	Risk assessment + authorisation (EU list of authorised substances)	Risk assessment + inclusion in a list of restricted or allowed substances	Risk assessments General provisions
What are regulatory consequences for substances identified as endocrine disruptors?						
Ban			Authorisation required		Assessment if criteria approved	

One Substance – One Toxicological Assessment?

- Critical considerations:
  - For some substances with a broad data package (e.g. pesticides) the strictest regulatory consequences (ban) are proposed while for other groups of substances with fewer data (and a higher level of uncertainty) less strict consequences may have to be applied
  - For hazard based regulations exposure may not have to be considered
  - It may be difficult to come to similar toxicological assessments for the same substance under different regulations (as illustrated by a few examples)

One Substance – One Toxicological Assessment?
Example 1 – isoflavones in food and feed



Isoflavones (e.g. formonenetin)

Sheeps on meadows with red clover

„Clover Disease“

- disturbance of fertility (reversible/irreversible)
- early aborts
- enlargement of uterus/udder

Isoflavones (e.g. genistein, daidzein)

Extracts, novel food etc.

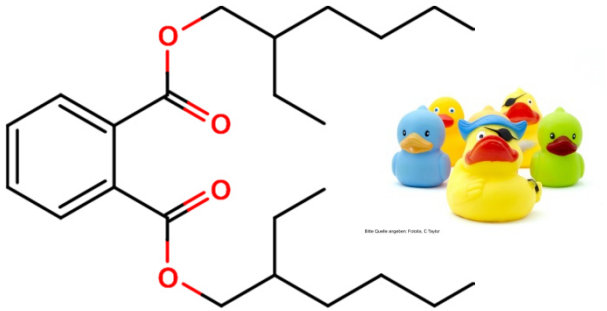
- High amounts of certain isoflavones
- No clarified safety for a longterm intake with high isoflavone dose

One Substance – One Toxicological Assessment? Example 1 – isoflavones in food and feed

For each of the several isoflavones, the aim one substance one toxicological assessment is difficult to achieve because:

- Different strength of evidence for ED effects by different isoflavones
- Classical toxicology (e. g. definition of NOAEL values) and hazard-based risk assessment do not fit for the risk evaluation of food supplements
- So far **no regulatory options** for endocrine active substances in food supplements (Regulation (EC) No 178/2002, Article 14 „**Food must be safe**“)

One Substance – One Toxicological Assessment? Example 2 – DEHP



Di(2-ethylhexyl)phthalate

DEHP as food contact material

Specific migration limit: 1,5 mg/kg food
Restrictions: plasticiser in repeated use materials and articles containing non fatty food…

DEHP as REACH chemical

Critical effect on the male reproductive system:
NOAEL = 5 mg/kg body weight per day
TDI (EFSA, 2005) = 0.05 mg/kg body weight per day

Mode of action: inhibition of testosterone production

DEHP – Not yet identified as human health ED under REACH

One Substance – One Toxicological Assessment? Example 2 – DEHP

For DEHP, the aim one substance one toxicological assessment is difficult to achieve because:

- DEHP is regulated under different pieces of legislation
  - E.g. as food contact material and industrial chemical under REACH
  - Different regulations contain different regulatory consequences for potential ED
- Without harmonized criteria applicable to all regulations the same substance may be regulated differently

One Substance – One Toxicological Assessment?
Example 3 – Copper compounds

Copper compounds as pesticide → Ban ?

Copper compounds as REACH chemical

SVHC candidate?

Testis atrophy observed in one study where copper was injected at high dose levels

Mode of action: unclear

Copper is also an essential metal and can be found in food

One Substance – One Toxicological Assessment? Example 3 – Copper compounds

For copper, the aim one substance one toxicological assessment is difficult to achieve because:

- Copper would be regulated under different pieces of legislation
  - E.g. as pesticide and industrial chemical under REACH
  - Different regulations contain different regulatory consequences for potential ED
- Without harmonized criteria applicable to all regulations the same substance may be regulated differently

One Substance – One Toxicological Assessment! Lessons learned from the examples

- Without scientific criteria for the identification and characterisation of endocrine disruptors in all fields of risk assessment of chemical and natural substances the goal one substance – one toxicological assessment is not achievable

- To come to such criteria several underlying controversies (e.g. on thresholds, non-monotonic-dose response curves) have to be solved

- Aim of the workshop is to look for potential compromises in these controversial issues

Goals and objectives

- Several open questions should be answered:
- Do EDC have a threshold?
- Is the level of uncertainty different from other substances?
- How can we identify EDC in a scientific and transparent way?

- There is a need for scientific advise to politics. Without scientific advise the decision on criteria might be driven by political issues alone.

Goals and objectives

- With this meeting we are striving to reach a consensus with all participants.
- The intended outcome is to refine the circulated draft text such that all participants can lend their names to it.
- We should be able to identify areas of agreement, together with topics where complete agreement cannot be reached.
- The results of this meeting can then be distributed to decision makers in the European Commission.
- The risk managers should assess whether any potentially remaining aspects of disagreement are actually policy relevant.

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Thank you for your attention

We are looking forward for a productive and constructive discussion!

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