FEDERAL INSTITUTE FOR RISK ASSESSMENT

BfR
Bundesinstitut für Risikobewertung

EU CONFERENCE ON ENDOCRINE DISRUPTORS

Criteria for Identification and Related Impacts

Potential Impacts Regarding Human Health Risk Assessment

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One Substance – One Toxicological Assessment!

But: - different regulations for chemical substances
- different data requirements (from all *in vivo* to *in vitro* only)
- different regulatory outcomes (from ban to not yet regulated)

Plant Protection Products (EC 1107/2009) / Biocidal Products (EU 528/2012)	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 toxicological data from manufacturers for the authorities available
What are the principle(s) of regulation?					
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 prohibited/ 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	not yet regulated

Principles for Evaluation for Human Health
of Substances with Effects on the Endocrine System

Category 1: Endocrine disruptors

- sufficient weight of evidence for **adverse effects** in humans at generally low dose levels with high regulatory concern for a **hazard-based management approach.**

Category 2: Suspected endocrine disruptors

- sufficient weight of evidence for **endocrine-mediated effects** in humans at generally moderate dose levels for a **risk-based management approach .**

Category 3: Endocrine active substances

- some evidence that substances affect the endocrine system, but **insufficient evidence for effects in intact organisms.**
- **Further examination** may eventually lead to allocation into Category 1 / 2 or even dispense from grouping.

Principles for Grouping for Human Health of Substances with Effects on the Endocrine System

- Considering the **complexity of the matter**, it is inappropriate to base grouping on the outcome of individual tests.
- Rather, **weight of evidence considerations and expert judgement** should be used case-by-case to decide on the grouping.
- Provided substances have undergone **comprehensive evaluation.**
- Current testing and assessment methodologies are generally suitable to derive **dose/concentration levels which can be considered safe**.
- There is no convincing evidence to assume that **levels of uncertainty** are generally different for EDs compared to other toxic substances.
- Based on **considerations on specificity, severity, reversibility, potency and consistency** of all effects **in a decision matrix grouping of substances** falling under the WHO/IPCS definition **is possible**.

IPCS Definition of Endocrine Disruption

An ED is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations (WHO/IPCS 2002).

IPCS Definition of Adversity

A change in morphology, physiology, growth, development or lifespan of an organism which results in impairment of functional capacity or imp
stress or increa
environmental

IPCS: International Programme on Chemical Safety of the WHO

ROADMAP: 4 Options for Criteria

Option 1:

No policy criteria continue to apply

Should not be applied in praxis

Option 2:

Hazard identification based on the WHO/IPCS definition

Prerequisite,
no stand-alone decision criterion

Step 1:
Identification

↓

Step 2:
Weight of evidence

↓

Step 3:
Characterisation and decision

Option 3:

Hazard identification and categories based on strength of evidence

Scientifically not sufficient

Option 4 (b), missing in the roadmap:

Hazard identification and hazard characterisation including severity of effects, reversibility, consistency and potency
(adapted from Kortenkamp et al. 2010)

Outcome of the BfR Impact Assessment Regarding Human Health Risk Assessment

Option 1:

- Not applicable
- Not reproducible
- 5 - 10 % of substances cut-off
- Not specific for ED, high number of false positive or negative decisions

Option 2

- Better applicability
- High reproducibility
- ~ 30 % of substances cut-off
- Low specificity (disregarding scientific information)

39 pesticide active substances

➢ reviewed by different scientists

➢ diverse options for decision making

Option 3 (not tested by BfR)

- Applicability assumed to be low
- Reproducibility assumed to be low
- % cut-off ?
- Low specificity assumed due to lack of definition for „strength of evidence“

Option 4 (b):

- **Best applicability**
- **High reproducibility**
- **5 - 10 % of substances cut-off**
- **High specificity**

Potential Impacts for Identification of Endocrine Effects Regarding Human Health Risk Assessment

Option 4 (b):

- **Best applicability**
- **High reproducibility**
- **5 - 10 % of substances cut-off**
- **High specificity**

Consequences:

- An ED decision matrix is needed, taking into account elements of hazard identification and hazard characterisation, such as
- severity, strength of evidence, reversibility, consistency and potency
- to obtain reliable, reproducible and transparent results.

Decision Matrix for Identification of Endocrine Effects Regarding Human Health Risk Assessment

Decision matrix	***Cat. 1***	***Cat. 2***	***Cat. 3***
Severity of effect(s)	severe	significant effects	limited effects
Strength of evidence	sufficient	sufficient	insufficient
Reversibility of effect(s)	(ir)reversible	reversible	not applicable
Consistency	high	medium-high	low
Potency for endocrine targets	high	low	not applicable

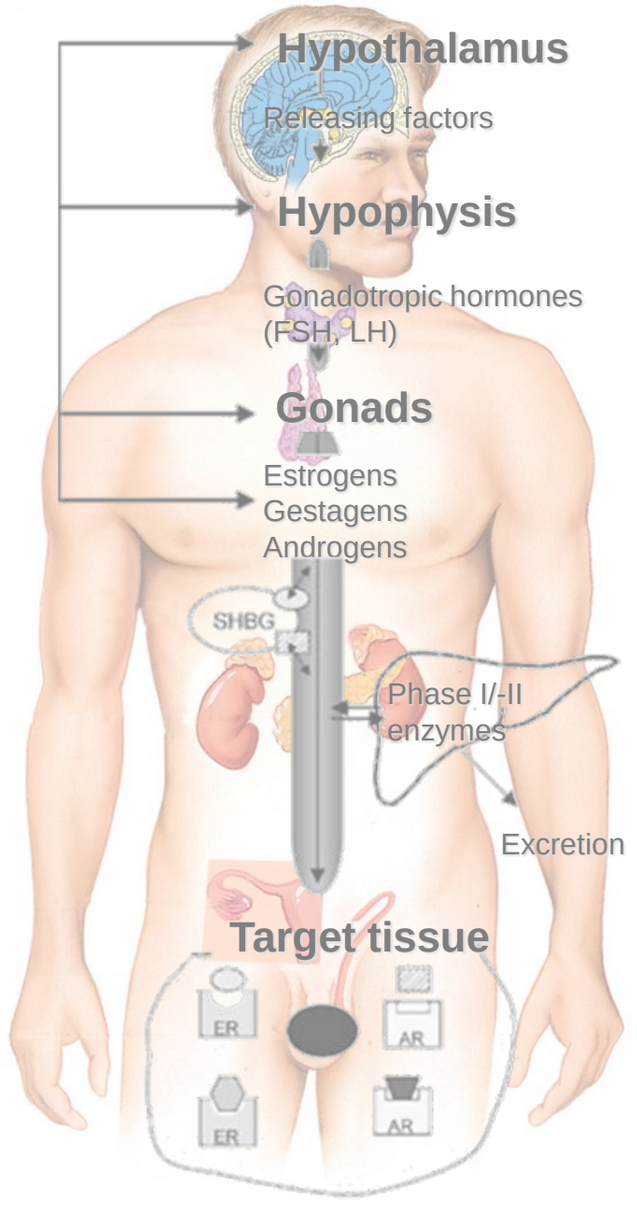
***Category 1: Endocrine disruptors*:** known or presumed human endocrine disruptor
***Category 2: Suspected endocrine disruptors*:** suspected human endocrine disruptor
Category 3: Endocrine active substances

Final Conclusions on Potential Impacts Regarding Human Health Risk Assessment

Strong support for option 4(b) as proposed by DE in 2013

Impacts:

- need of an **ED decision matrix**
- **reliable, reproducible, transparent**
- **science-based approach**
- **good applicability** and **acceptance**
- **compliance with international concepts**
- stop **inacceptable interim criteria**
- **high protection of human health**
- **safer use of pesticidal active substances**



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Thank you for your attention

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