Endocrine Disruptors – Overview of current situation in preparing legislation

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cefic

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Introduction

Cefic

- European Chemical Industry Council
- Committed to chemical safety and the protection of humans and the environment from harm caused by chemical exposure

  "Safe use of Chemicals"
- Committed to innovation (improved quality of life)
- Committed to sustainability (projected 9 billion people global population)
- Committed to competitiveness of the European chemical industry (energy, feedstock, regulation, IPR,…)

Peter Smith

- Executive Director for Product Stewardship and Fine, Specialty and Consumer Chemicals
- Industrial experience in Research and Development (consumer goods)
- Academic education in chemistry

Endocrine Disruptors (ED)

Industry Perspective

- Recognise that substances with endocrine disrupting properties are carefully controlled
  - Regulation to ensure consistency in applying safeguards and compliance to these standards

- Engagement of industry from the outset
  - A high priority amongst companies

Industry's Engagement on ED

Historical Perspective

1990s

- Weybridge Conference Recommendation (1996)
- EU Community Strategy (1999)

2000s

- WHO/IPCS Review/Definition (2002)
- OECD Testing Framework (OECD CF)
- Chemicals Regulation (REACH) acknowledges EDs (equivalent concern)

Industry's Engagement on ED

2010s

- Close collaboration with European Institutions (EU Commission)
  - JRC Expert Group (with MSCAs)
  - DG ENV Ad Hoc (Regulatory) Group (with MSCAs)
- Scientific Conferences (science ⇨ Regulation)
  - DG ENV conference (2012)
- European Parliament Own Initiative Report (2013)
- ECHA Expert Group with MSCA (started in 2014)
- Regulatory requirements
  - REACH review of Authorisation and ED (2013) – thresholds
  - Plant Protection Products (2013) – criteria
  - Biocidal Products (2013) – criteria
  - Cosmetics Regulation Review (2015) – criteria ?
  - Other sectors/regulations (Water, Medical Devices)
  - Outside Europe (SAICM emerging issue and US EPA)

ED - Scientific controversy

Useful References

- Kortenkamp et al: State of the Art Review (2012)
- WHO/UNEP Report (2013)
- EFSA Report (2013)
- Berlaymont Declaration (2013)
- Editors of Scientific Journals (2013)
- Scientists with opposing views/ Anne Glover meeting (2013)

Conclusion

No absolute scientific consensus on the best way to identify, characterise and risk manage ED

Industry Perspective

Kortenkamp et al (State of the Art Review)

- Not peer reviewed
- Selective referencing/interpretation
- Rhomberg et al critique available (Critical review in Toxicology, 2012; 42/6:465-473)

WHO

WHO/IPCS Report (2002)

- Balanced review
- Definition is now broadly accepted

WHO/UNEP Report (2013)

- Selected referencing
- Accompanied by « unrepresentative » executive summary (for “decision makers”)
- Lamb et al critique available (Regulatory Toxicology and Pharmacology, 2014; 69:22-40)

EFSA Scientific Opinion (criteria)

- Recognised the need for full hazard assessment when establishing regulatory criteria
- Hazard characteristics (potency, critical effect, severity, irreversibility)

Anne Glover Meeting

- WHO/IPCS definition accepted
- Safe (biological) threshold question left open

Risk and Hazard Applied to EDs

Hazard

- Identification of the potential of a substance to cause harm
  - Comes from a scientific understanding of the substance (agreed test methods etc.)

Risk

- Reality check that the potential harm is likely to occur under realistic conditions
  - Scientific understanding of the actual consequences of exposure to the substance at anticipated levels/duration

Society

- Need to be protected (from actual harm)
- Precautionary Principle (eliminate substances) balanced with Proportionality Principle (safely manage substances according to the risk of harm)

Regulatory Approaches

Regulation Type	Key Elements/Considerations
Hazard-based (eliminate the source of harm)	Hazard identification (necessary) - sufficient to avoid mistakes? Hazard characterisation (improves sufficiency; mistakes still made?) Derogations and exemptions (inevitable?)
Risk-based	Hazard characterisation and risk management options – Sufficient to ensure safety? – Exposure scenarios Case by case assessment (fewer or no exemptions/derogations)

(e.g. could energy-saving light bulbs be excluded from receiving an ecolabel due to trace of SVHCs?)

Industry supports a risk-based approach to safe chemicals management

- Scientific basis
- Weight of evidence approach (complex topics)

EU Regulation (Preparation)

3 Areas of Focus

Criteria

« How to recognise ED substances » (of regulatory concern)

Thresholds

Are safe exposure levels of ED substances possible? (REACH)

Strategy

Overall regulatory framework for handling ED substances

- choose between: minimising harm or minimising exposure

ED Criteria (Roadmap)

Original Objective

DG ENV to provide horizontal criteria by end of 2013 (for immediate adoption in the BPR and PPPR)

- Upfront stakeholder engagement
- No public consultation/Impact Assessment (IA)
- Only DG ENV proposal considered

Summer 2013

EU Commission (Secretariat General) intervened

Focus on BPR and PPPR (legal acts)

- Public consultation/IA
- Different policy options (« criteria ») to be assessed
- DG ENV and DG SANCO responsible

Spring 2014 (Industry understanding)

Roadmap constructed (DG ENV and DG SANCO)

- Consultation within the EU Commission
- Publication in 2-3 weeks possible
- Public consultation can start 2-3 weeks after roadmap consultation

ED Criteria (Roadmap) Industry Expectations

ECPA and Cefic

- Provided suggestions for Plant Protection (ECPA) and Biocidal Products (Cefic/EBPF)

Key Elements

- Criteria required (not categories)
- Hazard characterisation included (potency and others) within options
- Include risk assessment option with socio-economic considerations (regulation change of PPPR and BPR needed?)
- Assess impact on REACH/other regulations (optional)
- Assess “do nothing” option
  - Interim criteria (BPR + PPPR)
  - Case by case assessment/no criteria (REACH)

Commission Perceptive

- Flanker measures could emerge from the public consultation/IA (regulation change – e.g. to PPPR)

ED under REACH

Objective

- REACH requirement to clarify how ED substances are handled in the Authorisation process

Summer 2013

- Commission to provide a point of view on safe thresholds (Adequate Control and Socio-Economic Analysis (SEA) route)
  - Joint effort by DG ENTR and DG ENV

End 2013

- DG ENV presented key findings in CARACAL meeting
  - No change to the REACH regulation
  - ED substances covered by 57(f)
  - Thresholds can be taken into account if supported by scientific evidence (industry)

Spring 2014

- Formal Commission position presented at the CARACAL meeting (April) expected
  - SEA and Adequate Control routes open for ED substances in the Authorisation process (expected)

EU Community Strategy

Objective

- DG ENV to update the 1999 Community Strategy by end 2013
  - Reflecting latest scientific evidence/knowledge

Spring 2013

- JRC/DG ENV stakeholders groups (Experts and Ad Hoc) provide input to Strategy
  - Internal discussions within Commission to finalise Strategy document

End 2013

- Revised Strategy proposal (DG ENV) continues to be debated amongst Commission services
  - No final outcome yet
  - Priority appears to be given to the criteria (Secretariat General to advise)

2014

- Expect revised Strategy to be published (timing unknown)

EU Community Strategy Industry (Cefic) Perspective

Criteria

- Applied where they are appropriate (horizontal principle) – no categories
- Strategy publication should not pre-empt the outcome of on-going activities (e.g. development of criteria and assessment of policy options)

Risk Assessment

- Protect against harm (objective benefit focus) and not eliminate substances (chemical presence focus)
- Proof of adverse effect : not assumed (harm)
- Acknowledge safe thresholds can exist

New Science

- Combination effects (not ED specific)
- Non-monotonic effects (not ED specific)
- Chemicals in articles (not ED specific)

ECHA Expert Group

Human Toxicity	REACH Regulation
Environmental Toxicity	Biocidal Products Regulation

Industry Representation

- 4 representatives – to cover all 4 areas of interest (also PPPR expertise)
- 2 recognised substitutes (including cosmetics' expertise)
- Additional experts (as needed) to be confirmed

Provide expert guidance on ED substances (e.g. meet criteria for SVHC under REACH) to ECHA Member States Committee

- Expect final ED criteria to be used (criteria not legal requirement under REACH)

First meeting in February 2014; next meeting in May 2014

Industry – Supported Reports

WHO/UNEP Report

Critique : J.C. Lamb et al, 2014

Areas of Weakness

- Selective presentation of evidence
- ED over-emphasised as endpoint (when other risk factors could be implicated)
- Non-integration of exposure with toxicology and epidemiology
- Lack of consideration of exposure, dose, thresholds and potency
- No formal criteria for assessing causality

Overall

- Not objective, state of the art science review
- Not an update of WHO/IPCS 2002 report
- Causation tends to be inferred
- Weight of evidence approach largely ignored
- Points of controversy poorly covered
- Changes versus 2002 WHO/IPCS Report not explained
- Summary for decision-makers not a summary of full report

Industry Supported Reviews

Thresholds and Potency: (Review C.J. Borgert et al, Regulatory Toxicology and Pharmacology, 2013)

- Hormone activity produces biological potency thresholds
- Normal functioning of endocrine system requires potency thresholds
- Exogenous chemicals acting through hormonal mechanisms also have thresholds
- Endocrinology and endocrine pharmacology principles dictate potency thresholds
- An additive effect of background activity that precludes any safe level of exposure is inconsistent with endocrinology principles

Industry Supported Reviews

Kortenkamp et al "State of the Art Assessment"

(Critique: L.R. Rhomberg et al, 2012)

(Critical review in Toxicology, 2012; 42/6:465-473)

Weak Spots

- Well-intentional assessment, but falls well short of what is needed
  - Too ambitious for a single review
- Lacks a systematic evaluation of the literature
  - Selection criteria for inclusion/exclusion from the assessment unclear
- No objective assessment of strengths/ weaknesses of the specifically referenced studies
- No consistency check for different studies on the same substance
- Ignores dose-response considerations and does not follow a clear weight of evidence methodology
- Basis for changes in conclusions versus 2002 WHO/IPCS Report is not explained

European Parliament: Own Initiative Report (2013)

The European Parliament's Own Initiative Report states that a comprehensive hazard assessment should be included in the ED criteria.

- Hazard Assessment includes both hazard identification and hazard characterisation
- Hazard Characterisation recognised by EFSA as having to be evaluated to inform on "level of concern"

The EP Own Initiative Report rejected the idea that potency should not be included in the criteria:

« Strongly disagrees with the attempts to introduce the criteria of "potency" as a cut off for the definition of ED, as this would unduly limit the definition of ED, and make it scientifically flawed and not coherent with the classification of Carcinogenic, Mutagenic and Reprotoxic substances which is based on strength of evidence. »

The EP Own Initiative Report states that ED substances should be regarded as non-threshold with manufacturers needing to provide evidence to the contrary.

EFSA Scientific Opinion : Criteria for ED

ED Definition

- Adverse effect in an intact organism/(sub)population
- Endocrine activity
- Plausible causal relationship

Adversity Assessment

- Scientific criteria not generally defined
- Expert judgement required in a weight of evidence approach

Testing Framework

- Standardised assays reasonable complete for EATS modalities
- Birds and amphibians less well covered

ED Hazard Characterisation

- Requires: critical effects, severity, (ir)reversibility, and potency

Hazard and Risk Assessment

- To inform on risk and level of concern, risk assessment makes the best use of available information (hazard and exposure)
- ED treated like other substances of concern and subject to risk assessment and not only hazard assessment

EFSA Scientific Opinion : Criteria for ED

Non-ED Specific Considerations

Critical Windows of Susceptibility

- In vivo required to encompass sensitive life stages
- OECD conceptual framework covers exposure during critical periods of development, but not all

Combined Exposure to Multiple Substances

- Recognition that exposure to multiple endocrine active substances could lead to combined activity
  - Mixture toxicity requires more research (not uniquely in an ED context)

Low Dose Effects and Non-Monotonic Dose Response Curves

- Recognition of lack of scientific consensus on existence/relevance of low dose effects in relation to EDs.

Biocides Product Regulation (BPR)

Interim Criteria (already in effect; December 2013)

- Carcinogen C2 and Reprotoxic R2 (C2 + R2)
- Reprotoxic R2 only (need to show toxic effect on endocrine organs)
  - MSCA (judgement) + ECHA Expert Group (referral)

Cefic stresses the need to apply the WHO/IPCS definition + risk assessment

Derogation (Article 5 of BPR)

At least one of the following must apply:

- Risk under realistic worst case conditions is negligible (e.g. closed system)
- Active substance is essential to present/control a danger to human health or environment
- Non-use leads to a disproportionate (negative) impact on health versus use.

Thank you for your attention