Endocrine Disrupting Substances

Impact on Crop Protection and Agronomic Effects

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Determination of *endocrine disrupting properties*

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- The Commission's policy should fit with its overall objective of ensuring a high level of protection for human health and the environment.
- Industry is committed to safety of products.
- Our industry takes society´s concerns regarding endocrine disruption extremely seriously.
- Existing test methods are under constant improvement (OECD, EFSA).
- Identification of an endocrine disruptor relies on a weight of evidence approach: endpoints from many studies are integrated in making a judgement, including the potential for toxicity during 'critical windows' of exposure or 'vulnerable' periods in a life stage.

ED regulation in the EU

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ENVIRONMENT

Horizontal ED criteria for all sectors

HEALTH AND CONSUMERS

Pesticides
Hazard-based cut-off
Limited derogations possible
ED criteria: proposal by December 2013

ENVIRONMENT

Biocides
Hazard-based cut-off
Derogations possible
ED criteria: adoption by December 2013

ENVIRONMENT

REACH
ED may be SVHC
Authorisation based on risk assessment
ED criteria: no legal requirements

- **Harmonized criteria, but consequences differ**

EU Policy making for PPP based on hazard – not risk

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Hazard

- Hazard: Potential source of harm or adverse health effect on a person or the environment
- Substances regulated on basis of their intrinsic properties (pesticides are made to control and destroy…)
- Hazard based cut-offs do not allow for risk assessment

Risk

- Risk = Hazard x Exposure
- Exposure elements
- ‘The dose makes the poison’

Background - Regulation 1107/2009

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- **Endocrine disruption a hazard based cut off criteria**
- **Annex II, Article 3.6.5, Article 3.8.2**

  An active substance … shall only be approved if, … it is not considered to have ***endocrine disrupting properties*** *that may cause adverse effects in humans/non-target species.*

  By [13 December 2013], *the Commission shall* ***present*** *… specific* ***scientific criteria*** *for the determination of* ***endocrine disrupting properties****…*

- **Until then interim criteria apply**
  - C2 & R2
  - R2 & toxic to endocrine organs

Background - Regulation 1107/2009

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Interim criteria

- Pending the adoption of these criteria, substances that are or have to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogenic category 2 and toxic for reproduction category 2, shall be considered to have endocrine disrupting properties.

– Interim criteria not scientifically justified (not all substances classified as C2 and R2 are automatically endocrine disrupters)

– No interim criteria and legislative deadline for the environment

– Interim criteria are beeing applied for the CfS list

– Some member states want to apply interim criteria for AIR2

– ECPA position: interim criteria should not be applied for regulatory decision making

Provision is a poor substitute for scientific criteria

Development of ED criteria

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DG Env proposal – mid 2013

- Released for bilateral discussions (draft recommendation)
- 2 regulatory categories, analogous to CMR
- Concept based on degree of evidence

1	Endocrine disruptor	**Known** to cause ED mediated adverse effects in: (1) human data or env field data, or (2) evidence from laboratory animal studies
2	Suspected endocrine disruptor	**Some** evidence for ED mediated adverse effects (human/env field data or laboratory animal studies) but evidence "not sufficiently strong" for Cat 1

- Potency, severity, (ir)reversibility, lead toxicity excluded
- No commitment on where regulatory line will be drawn

Development of ED criteria

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ECPA comments on DG Env proposal

- Aim should be to catch **substances of concern**
- **ED's can be treated like most other substances**
- **Risk assessment** should be basis for assessing & managing endocrine active substances
- Categorisation concept :
  - Legislation requires criteria not categories
  - Potential blacklisting and subsequent impacts
  - Scientifically ED is not analogous to CMR
- Recommended single set of horizontal ED criteria to distinguish substances of high concern from low concern
- ED = only those substances with clear adverse effects mediated via accepted endocrine MOA and considering relevance, lead toxicity, **potency**, severity → following a **WoE approach**

EFSA

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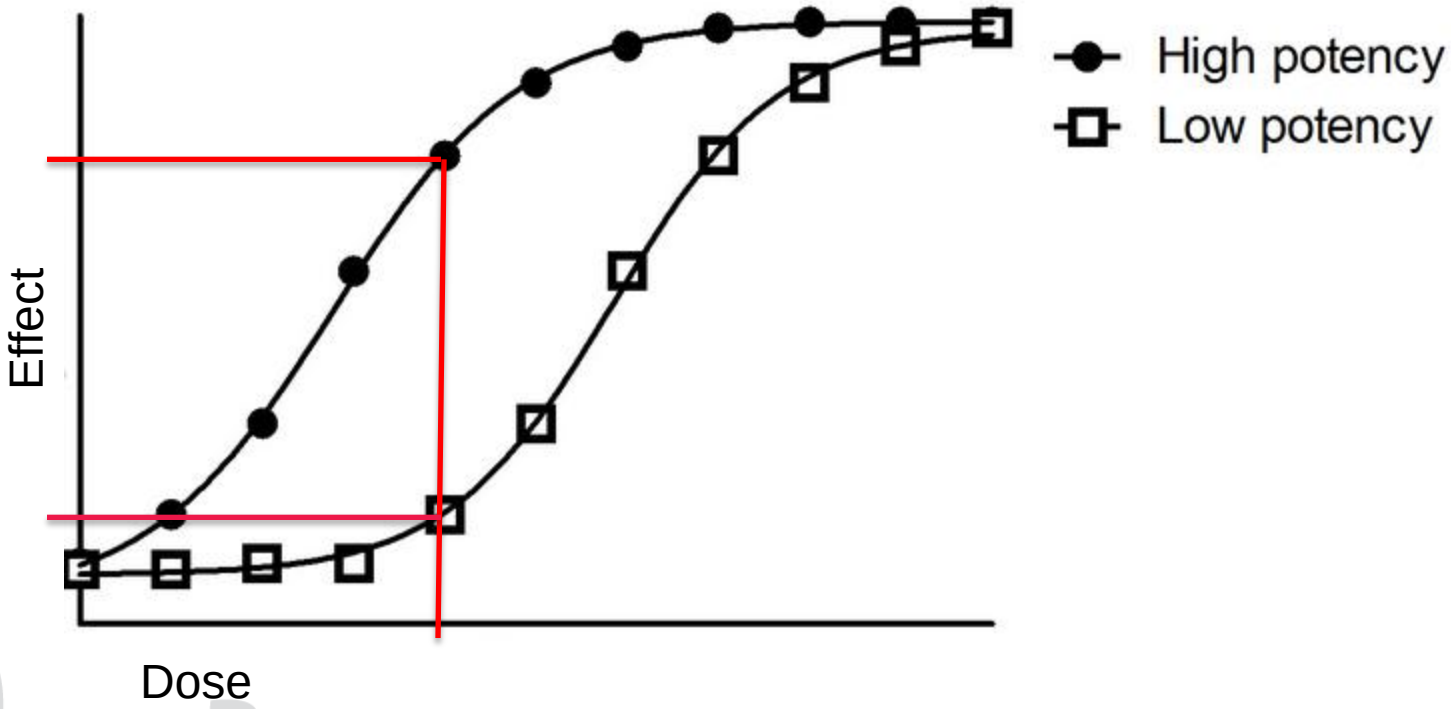
"Critical effect, severity, (ir)reversibility and **potency** aspects are part of the hazard characterisation of EDs. To inform on risk and level of concern for the purpose of risk management decisions, **risk assessment makes best use of available information**"

EFSA Opinion, March 2013

Potency is key



Same dose – different effect!!

Industry view on the ED criteria

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The criteria should…

- be based on the widely accepted WHO definition
- include elements of hazard characterization (e.g. potency, severity, lead toxic effect, irreversibility)
- be a single set of criteria as required by the legislation (and not a categorization)

Hazard idenfication (WHO definition; adverse effect and ED MoA)	Hazard characterization	Exposure characterization	Risk assessment

DG Envi proposal — Some MS — US EPA, EFSA, Industry

Member States voices

- **UK**: “adversity is key in the identification of an endocrine disruptor (as per the IPCS definition). […] failure to take potency into account creates **inconsistencies** with the way that the current regulatory system considers the science […].
- **Ireland**: “Are we really suggesting that a substance toxic at nanogram amounts **is of the same level of concern** as one active at kilogram doses?”

DK EPA proposal

Danish Ministry of the Environment
Environmental Protection Agency

Category 1: Confirmed ED

- Adverse *in vivo* effects & ED MoA highly plausible
- ED MoA *in vivo* clearly linked to adverse effects *in vivo* (e.g. by read across)

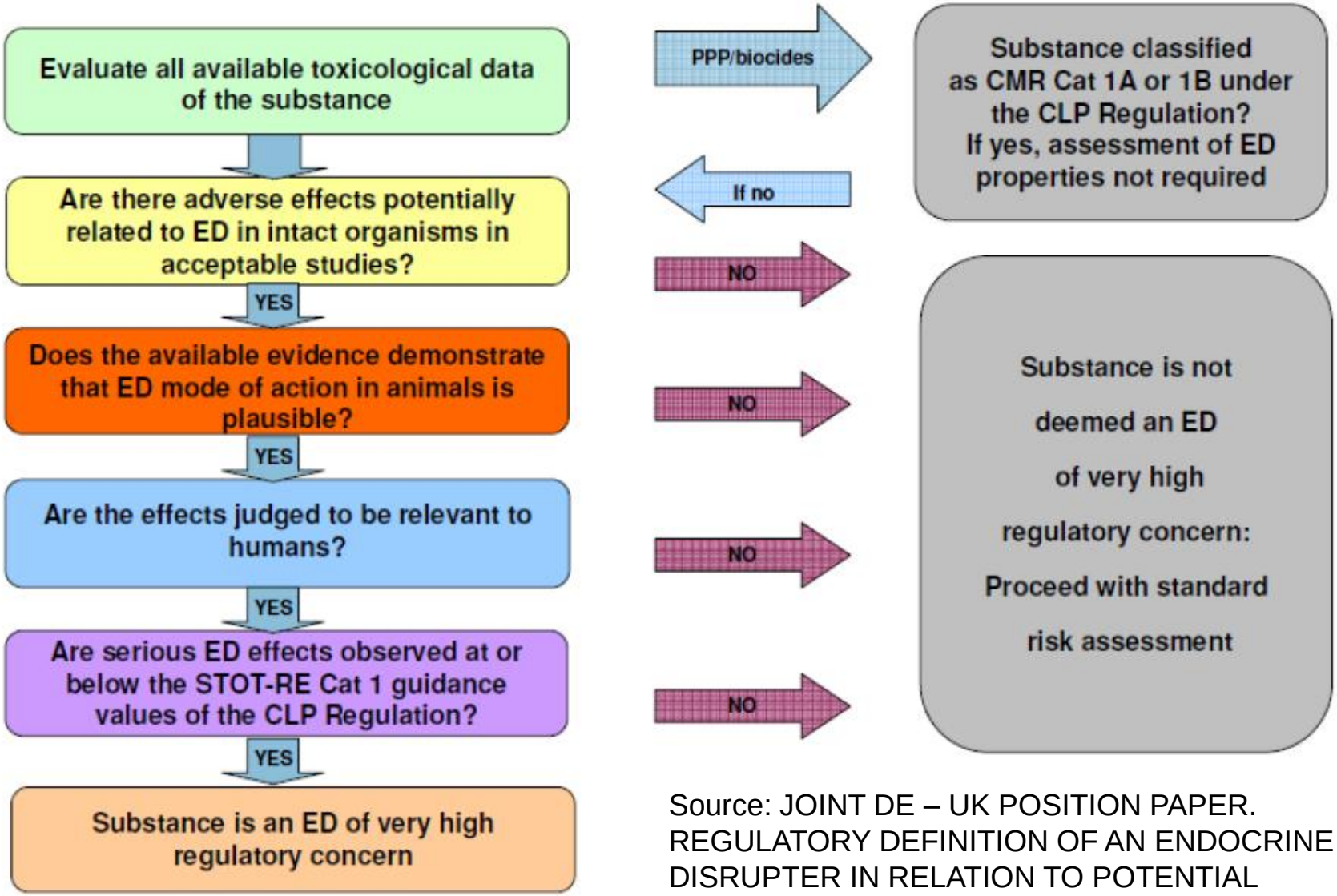
Category 2a: Suspected ED

- Some evidence, mainly based on *in vivo* data

Category 2b: Indicated ED

- Some *in vitro/ in silico* evidence indicating an ED potential

BfR/ CRD proposal (human health)



Source: JOINT DE – UK POSITION PAPER. REGULATORY DEFINITION OF AN ENDOCRINE DISRUPTER IN RELATION TO POTENTIAL THREAT TO HUMAN HEALTH. May 2011.

ECPA impact assessment

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Scope

- Based on the proposal by DG Environment (February 2013)
- Impact on agriculture, trade and future innovation

Key messages

– 35 - 45 % of the European crop protection market will be affected (3-4 billion €)

– Fungicides are particularly vulnerable: The ten most important cereal fungicides in Germany would be lost, in France 7 out of the top 10 products would be removed

– Yield losses on key crops would be 8-10% (OSR), 10-20 % (wheat) in an average year and up to 50 % in years of high disease pressure

– Significant impact on innovation and international trade

Substances that could be affected by criteria

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- **Evaluation based on PSD (UK) evaluation in 2008**

  37 substances identified

- **But based on DG ENV criteria expected impact is much greater!**

  Could affect all substances in some chemical classes

ASs most likely to be eliminated		
Substance	**Expiry of approval**	**Market value**
Insecticides		
• Thiacloprid	12/2014	61
Fungicides		
• Cyproconazole	05/2021	65
• Epoxiconazole	04/2019	208
• Fenbuconazole	04/2021	2
• Iprodione	10/2016	16
• Mancozeb	06/2016	130
• Maneb	06/2016	5
• Metconazole	05/2017	63
• Tebuconazole	08/2019	151
Herbicides		
• Amitrole	12/2015	-
• Ioxynil	02/2015	15
• Molinate	07/2014	5
European market value 2011		*621*

ASs which may be eliminated		
Substance	**Expiry of approval**	**Market value**
Insecticides		
• Deltamethrin	10/2016	47
• Dimethoate	09/2017	38
Fungicides		
• Difenoconazole	12/2018	38
• Folpet	09/2017	46
• Fluquinconazole	12/2021	4
• Fuberidazole	02/2019	-
• Metiram	06/2016	12
• Myclobutanil	05/2021	29
• Penconazole	12/2019	31
• Prochloraz	12/2021	56
• Propiconazole	01/2017	108
• Prothioconazole	07/2018	304
• Tetraconazole	12/2019	16
• Thiram	07/2014	13
• Triademenol	08/2019	22
• Triticonazole	07/2017	3
Herbicides		
• 2,4-D	12/2015	49
• Carbetamide	05/2021	3
• Chlorotoluron	02/2016	20
• Fluometuron	05/2021	3
• Metribuzin	09/2017	32
• Picloram	12/2018	7
• Tepraloxydim	05/2015	6
• Triflusulfuron	12/2019	42
Other		
• Metam	06/2022	34
European market value 2011		*963*

Impact on innovation
Current situation in the EU

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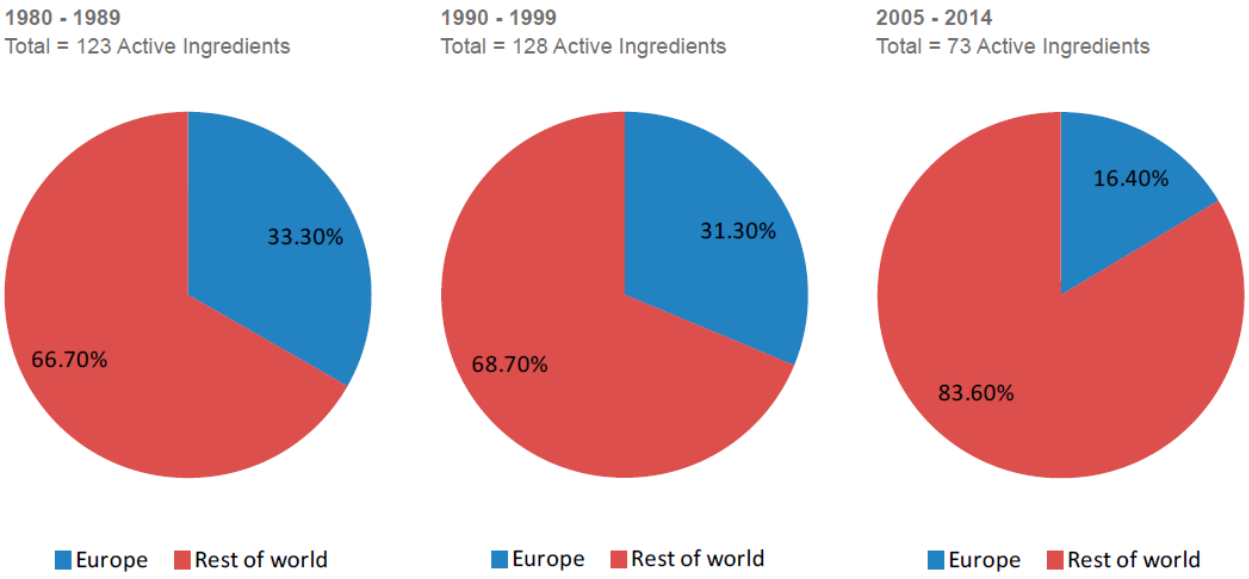
Active ingredients in development (worldwide)

Share of active ingredients introduced or in development

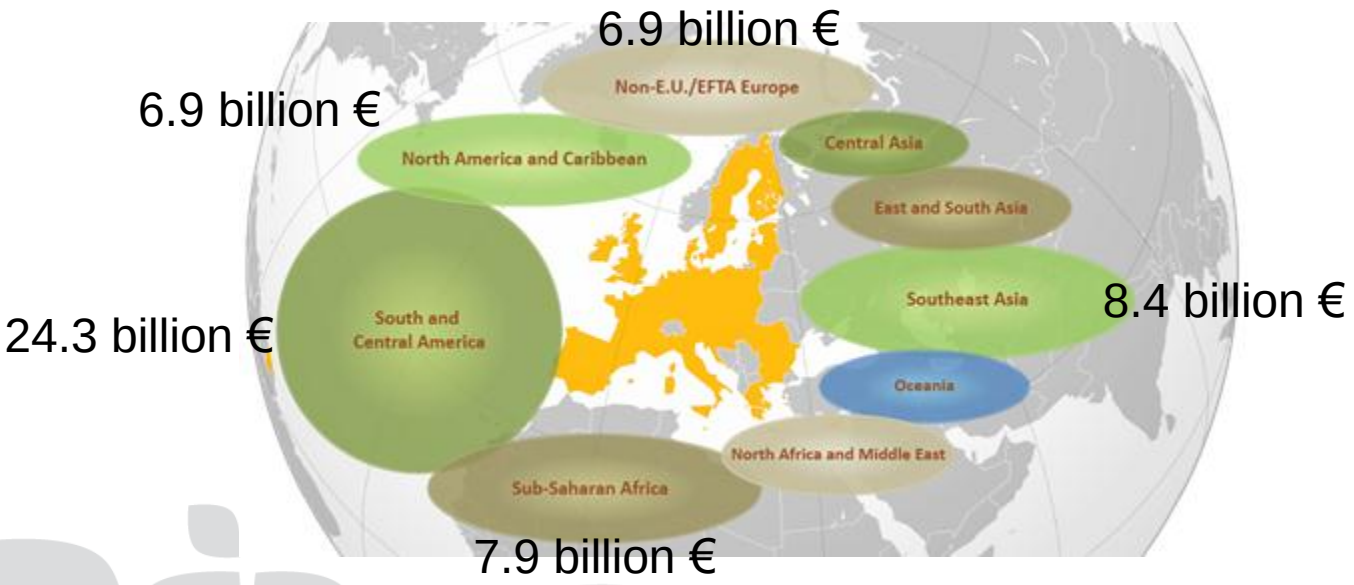


- **ED criteria have the potential to further hinder innovation and research in the EU**

Source: R&D trends for chemical crop protection products and the position of the European Market. A consultancy study undertaken for ECPA. Phillips McDougall, September 2013

Impact on international trade

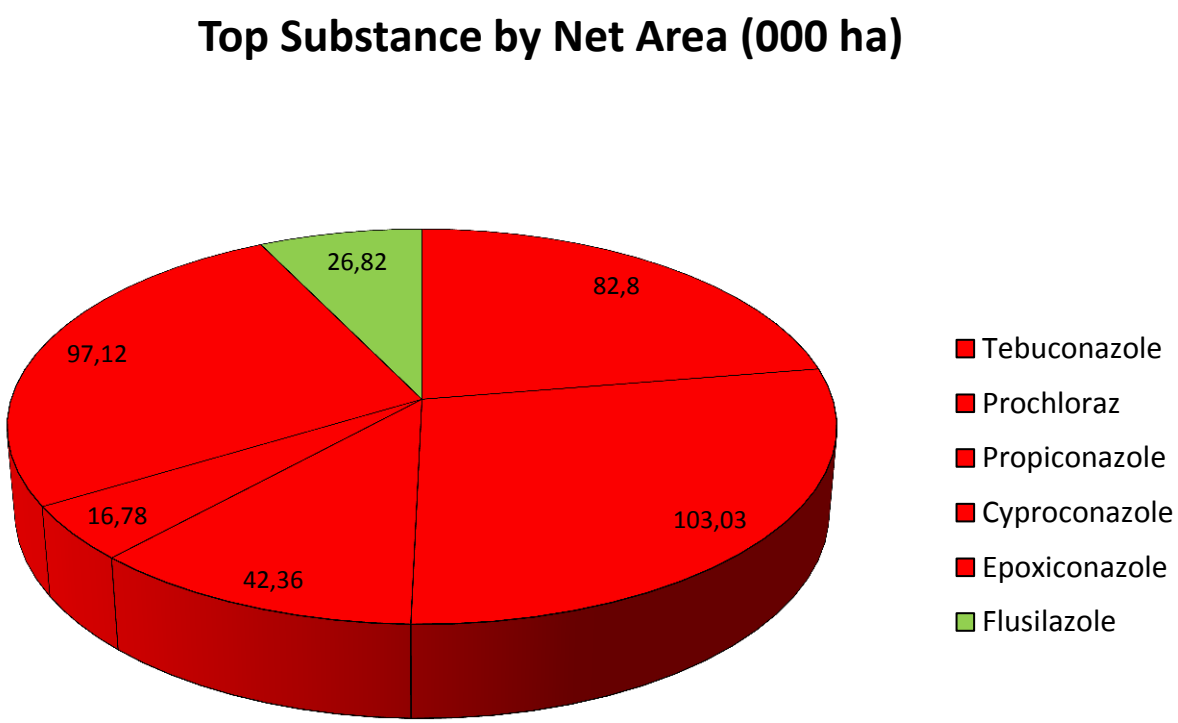
- Based on the assumption that all MRLs will be set at the default value of 0.01 mg/kg
- Imports worth 65 billion € would be affected by ED cut-off criteria alone



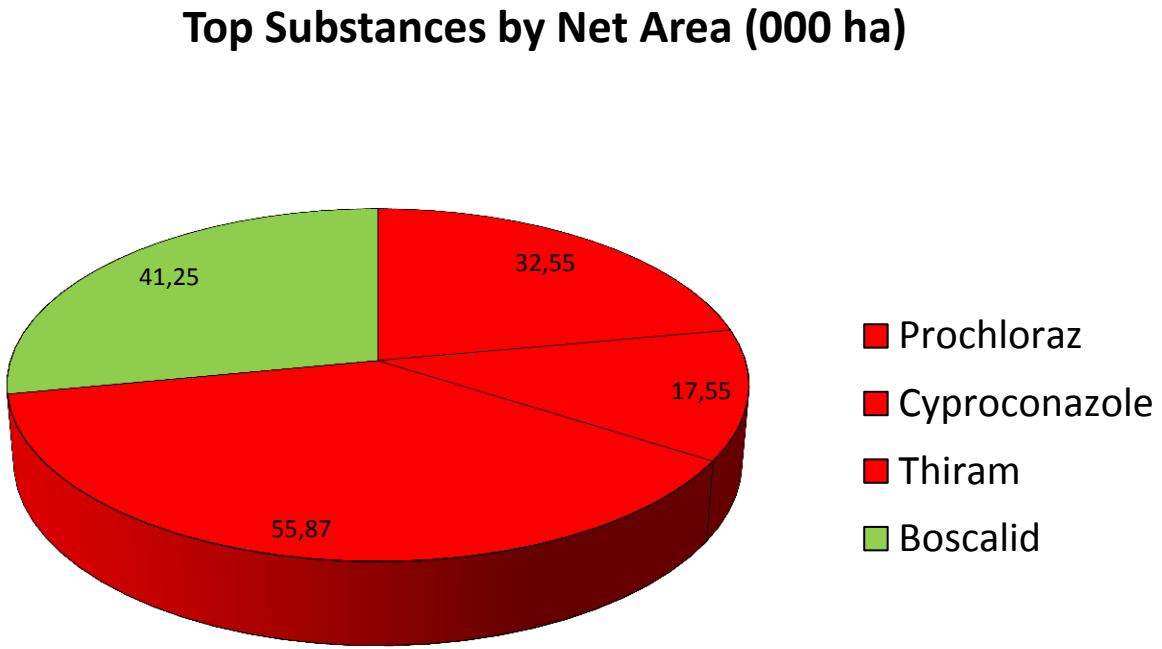
Source: Potential Trade Effects on World Agricultural Exporters of European Union Regulations on Endocrine Disruptors. Prepared by Kyd D. Brenner LLC for CropLife International, February 2014.

- Huge potential impact on international trade

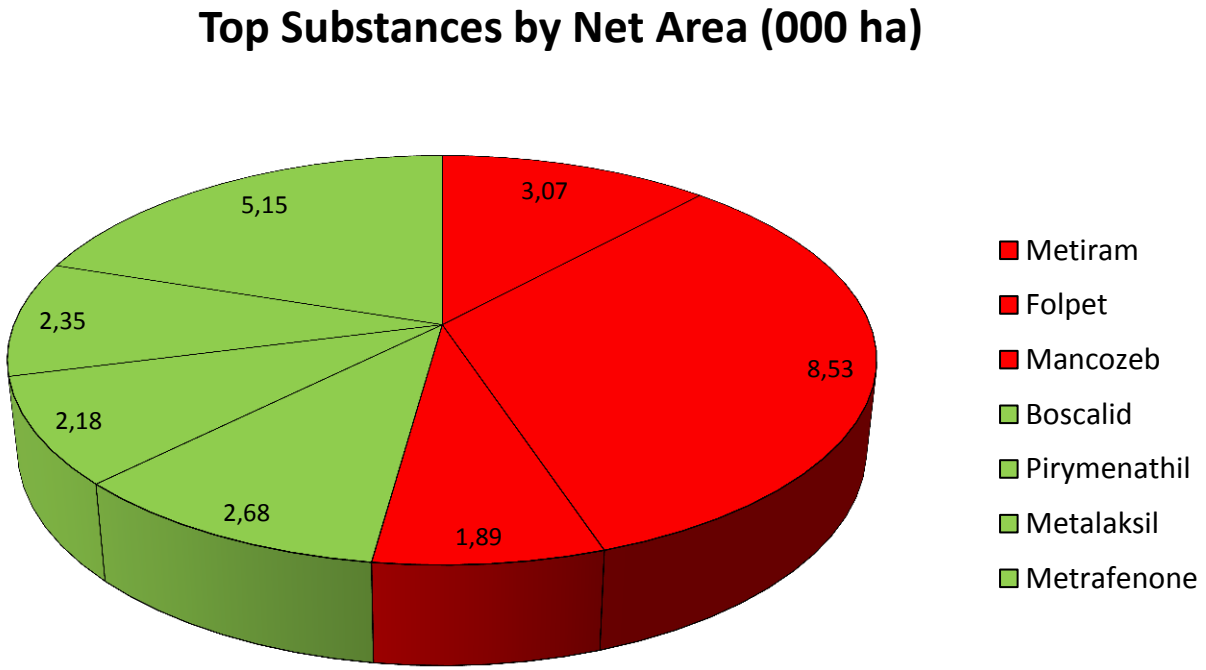
Active Substances for Slovakia, Cereals, Top 10 Fungicides (2012)



Active Substances for Slovakia, Sunflower, Top 10 Fungicides (2012)



Active Substances for Slovakia, Vine, Top 10 Fungicides (2012)



Summary

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- ECPA takes ED-related concerns seriously and believes that they can be addressed using a science and risk-based approach
- The WHO definition and elements of hazard characterization should be the basis for the criteria
- DG Environments‘s proposal would have had a significant negative impact on European agriculture, innovation and international trade
- The Commission impact assessment offers the chance to provide a more solid basis for the ED criteria and the revision of the ED strategy

Back- Up

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Expert Advisory Group (EAG)

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Members

- Experts from member states authorities, industry and NGOs
- EU agencies (EFSA, ECHA) & COM services as observers
- Chaired by the Joint Research Centre (JRC)

Final Report

- Hazard identification: Consideration of mode of action and adversity in parallel applying weight of evidence
- Human health: Potency, severity, irreversibility and lead toxicity are relevant for hazard characterization
- Environment: Adverse effects must be population relevant

EFSA Scientific Opinion

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- **Joint work with experts from EMA, ECHA, EEA**
- **Mandate by COM, published in March 2013**
  - Reasonably complete set of standardised assays for EATS in mammals and fish are available
  - Critical effect, severity, (ir)reversibility and potency are part of hazard characterization of EDs
  - Mixture toxicity and low-dose effects are not unique for EDs
  - Risk assessment makes best use of available information

efsa

- **EDs can be treated like most other substances of concern for human health and environment**