Endocrine discuptors under REACH

8. BfR Forum Verbraucherschutz

"When substances affect the endocrine system – Possible health risks of endocrine disruptors"
20-21 April 2010

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ECHA – Classification Unit

Outline

- ECHA's role under REACH and CLP
- ED in REACH main processes
    - Registration
    - Evaluation
    - Authorisation
    - Restriction
- Further information
- Conclusion

ECHA – the coordinator of REACH and CLP implementation

MISSION

- Manage REACH and CLP tasks
- Ensure a consistent implementation at EU/EEA level
- Provide with the best possible scientific advice on safety and socio-economic aspects of the use of chemicals
- Ensuring a credible decision-making process, using the best possible scientific, technical and regulatory capacities
- Manage guidance, IT tools and data bases
- Support national helpdesks and provide advice to registrants
- Make info on chemicals publicly accessible

ORGANISATION

- Management Board
- Executive Director
- Secretariat (currently staff of 382*)
- Three Scientific Committees
- Forum on Enforcement
- Networks (Help Net, RCN, SON)
- Board of Appeal

*As of 15.04.2010

Objective of REACH

ECHA
European Chemicals Agency

Article 1:

- The purpose of this Regulation is to ensure a **high level of protection of human health and the environment**, including the promotion of alternative methods for assessment of hazards of substances, as well as the **free circulation of substances on the internal market** while enhancing competitiveness and innovation.
- This Regulation is based on the principle that it is for manufacturers, importers and downstream users **to ensure that they manufacture, place on the market or use such substances that do not adversely affect human health or the environment**. Its provisions are underpinned by the precautionary principle.

Endocrine disruptors in REACH Legal text

- Endocrine disrupting properties/potential:
  - Article 57 (authorisation) and 138 (review by COM)
  - Annex II (SDS)
- Equivalent level of concern
  - Article 49 (intermediates)
  - Annex I (CSR – PBT assessment)
  - Annex XV (dossiers)

ED Definition

- No definition in REACH, not addressed in CLP
- Weybridge (1996)
- WHO/IPCS (2002)
- REACH guidance* refers to Community strategy for endocrine disrupters:

  "An endocrine disrupter is an **exogenous** substance or mixture that alters function(s) of the endocrine system and consequently can cause **adverse** health effects **in an intact organism**, or its progeny, or (sub)populations"

*Guidance for the preparation of an Annex XV dossier on the identification of substances of very high concern**)**

REACH processes

- Pre-registration
- Data sharing
- Registration

Industry gathers information and ensures responsible and well-informed management of the risks

ECHA

MSs

- Evaluation
  - Dossier evaluation
  - Substance evaluation

ECHA and MS-CAs control and request for further info

- Authorisation
- Restriction
- Classification & labelling

COM, with support of ECHA and MS-CAs, applies community wide risk management systems

Information requirements under REACH

No testing for endocrine disruption specified - but

in order to identify the absence or presence of hazardous properties the registrant should gather

- **all existing available test data** on the substance to be registered,
- **all other available and relevant information on the substance**
  - **regardless whether testing for a given endpoint is required or not at the specific tonnage level**.
  - **including information from alternative sources (e.g. from (Q)SARs, read-across from other substances, *in vivo* and *in vitro* testing, epidemiological data)**

OECD Conceptual framework

Level 1: Sorting and prioritisation based upon existing information

Level *2: In vitro* assays providing mechanistic data

Level *3: In vivo* assays providing data about single endocrine mechanisms and effects

Level *4: In vivo* assays providing data about multiple endocrine mechanisms and effects

Level *5: In vivo* assays providing data on effects from endocrine and other mechanisms

OECD Conceptual framework

Data potentially available under REACH

Level	Data: Human health	Data: Environment
1. Sorting and prioritisation based upon existing information	1. Phys-chem, production volume, release, use pattern, available tox data	
2. *In vitro* assays providing mechanistic data	2. **QSARs, ER, AR, TR receptor binding...**	2. **Fish hepatocyte VTG* assay, QSAR**
3. *In vivo* assays providing data about single endocrine mechanisms and effects	3. **Uterotrophic assay, Hershberger assay,**	3. **Fish VTG assay,**
4. *In vivo* assays providing data about multiple endocrine mechanisms and effects	4. **Enhanced OECD TG 407, pubertal assays, adult intact male assay**	4. **Fish gonadal histopathology assay, frog metamorphosis assay**
5. *In vivo* assays providing data on effects from endocrine and other mechanisms	5. **Repro screening test (OECD 421/422) enhanced 1 or 2-gen study (OECD 415, 416)**	5. **Partial and full life cycle assays in fish, birds amphibians and invertebrates**

*VTG=Vitellogenin

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Dossier Evaluation

- Examination of testing proposals (REACH, Art. 40): After public consultation and considering all scientifically valid information and studies received, ECHA can
  - Accept
  - Reject or
  - Modify the testing proposal
    (Test conditions, additional test(s) in case of non-compiance)

Evaluation against REACH standard information requirements (ECHA)

- Compliance check (REACH, Art. 41)

Substance evaluation

- REACH Art. 44-54
- Substance prioritised for Community Rolling Action Plan (CRAP; ECHA)
  - Hazard
  - Exposure
  - Aggregated tonnage
  - …
- MS performs, ECHA coordinates

→ Request of information data beyond standard information requirements possible!

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Authorisation (REACH Art. 57)

Substances to be included in Annex XIV:

(a) – (c) CMR cat 1 or 2

(d) PBT (Annex XIII criteria)

(e) vPvB (Annex XIII criteria)

(f) substances— **such as those having endocrine disrupting properties** or those having persistent, bioaccumulative and toxic properties or very persistent and very bioaccumulative properties, which do not fulfil the criteria of points (d) or (e) — for which there is scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e) and which are identified on a case-by-case basis in accordance with the procedure set out in Article 59

The authorisation procedure: a 2-step approach

- Step 1: Subjection of substances to authorisation requirement

- Step 2: Authorisation applications and decisions

Authorisation Step 1 : The selection of substances for authorisation

This step covers:

- Identification of SVHCs → **"*candidate list*"**
  Who?: MSCAs / Commission; ECHA (Secretariat + MSC)
  + public consultation

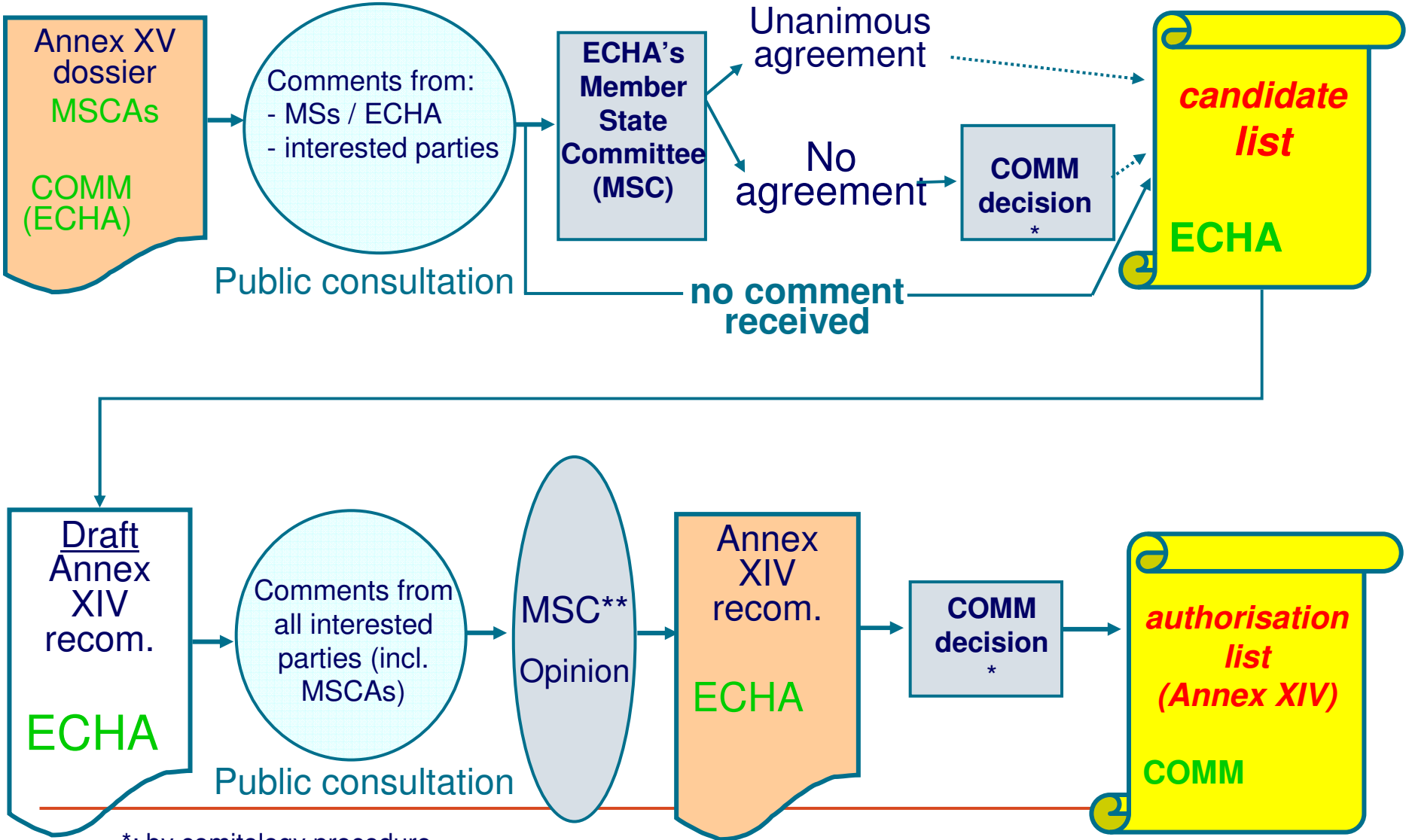
– Prioritisation of substances → **"*recommendation*"**

Who?: ECHA (Secretariat + MSC) + public consultation

– Inclusion in Annex XIV → **"*authorisation list*"** (Annex XIV)
Who?: Commission

Main actors: public authorities

Selection of substances for authorisation



*: by comitology procedure

**:MSC=Member State Committee

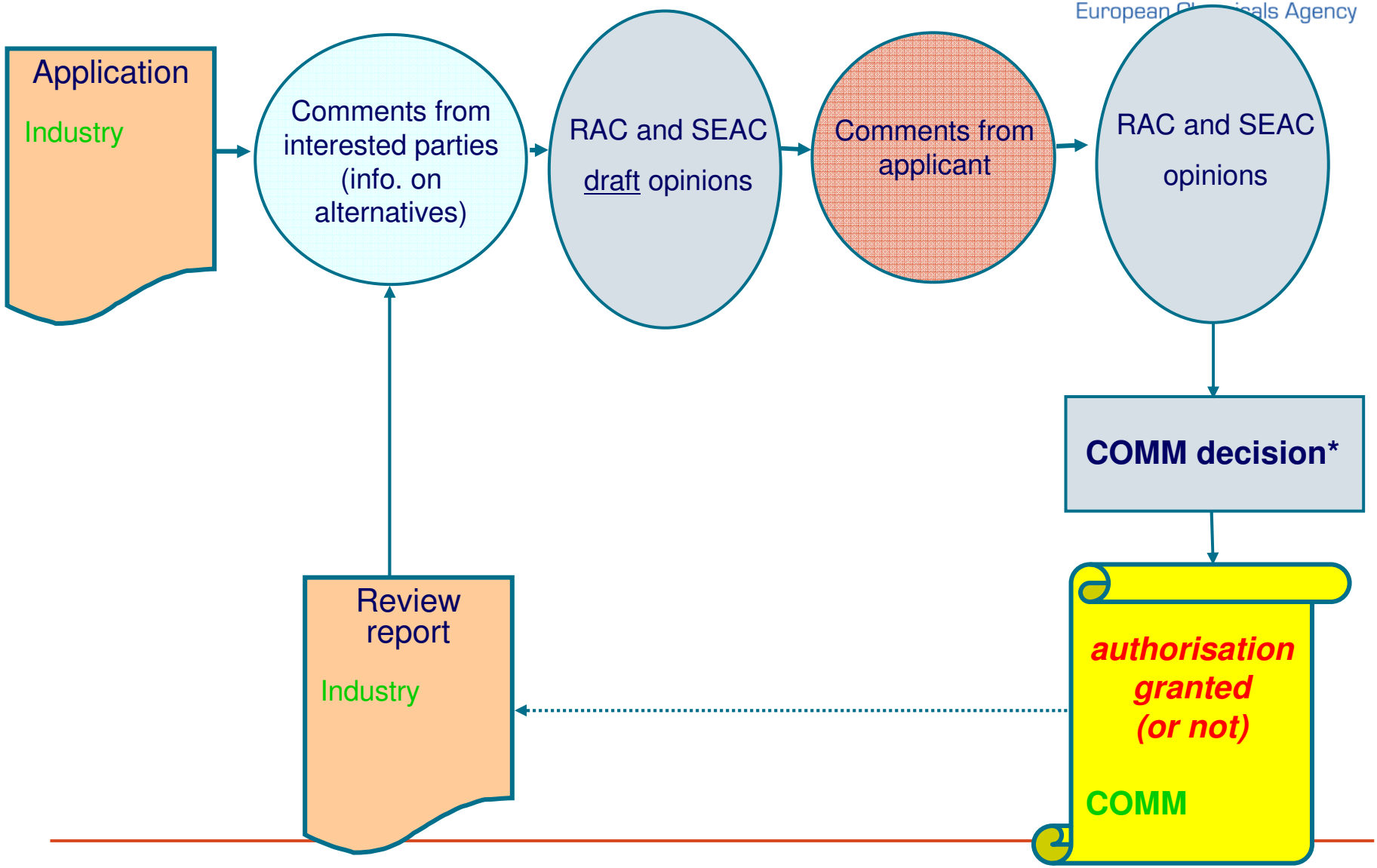
Authorisation Step 2:
The authorisation applications and decisions

This step covers:

- the application for authorisation (industry)
- the granting of authorisation (Commission, on the basis of ECHA's scientific committees* opinions)
- the review of authorisations (industry / ECHA's scientific committees / Commission)

*: RAC: Risk Assessment Committee / SEAC: Socio-Economic Analysis Committee

2. The authorisation applications and decisions



*: by comitology procedure

Granting authorisations

- The Commission **shall** grant an authorisation if:

  risks are adequately controlled (« adequate control route »)

  !NB: not applicable for substances with PBT, vPvB properties and non-threshold CMs

- The Commission **may** grant an authorisation if:

  socio-economic benefits outweigh the risks

  and

  there are no alternatives available that

  (1) reduce the overall risk and

  (2) are technically and economically feasible

  (« socio-economic route »)

Article 13: Review

- …
- 7. By 1 June 2013 the Commission shall carry out a review to assess whether or not, taking into account latest developments in scientific knowledge, to extend the scope of Article 60 (3) (socio-economic route) to substances identified under Article 57(f) as having endocrine disrupting properties. On the basis of that review the Commission may, if appropriate, present legislative proposals.

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Restrictions framework

Definition of restriction (Art 3.31)

- Restriction - means any condition for or prohibition of the manufacture, use or placing on the market

Restrictions may be imposed on (Art 67 and 68):

- manufacture, use and/or placing on the market
- a substance on its own, in preparation or in an article

When

- an unacceptable risk to human health or the environment
- this risk needs to be addressed on a Community-wide basis

General exemptions (Art 67)

- scientific research and development
- risks to human health due to use in cosmetic products (dir 76/768/EEC)
- on-site isolated intermediates

Characteristics

- Continues the work done under Directive 76/769/EEC
- A safety net where other REACH processes do not ensure adequate control of risks
  - registration (CSR, RMM, operational conditions)
  - downstream obligations
  - possible dossier and/or substance evaluation

  and authorisation under REACH or other Community actions are not more appropriate
- MSs or ECHA on request of the Commission
- Community-wide action: the same requirements apply to whole EU
- Flexible instrument

Restriction vs authorisation

- **Authorisation**: industry is not allowed to place on the market or use a substance included in Annex XIV unless industry has an authorisation granted by the Commission

- **Restriction**: industry has to comply with the conditions of the restriction in Annex XVII for the substance,

  no specific dossier submitted

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CLP Regulation

- Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging entered into force on 20 January 2009
- Replaces
  - Directive 67/548/EEC (Dangerous Substances Dir., DSD)
  - Directive 1999/45/EC (Dangerous Preparations Dir., DPD)
  - REACH, Title XI (Classification & Labelling)
- Transitional period 2010 – 2015
  - Both classification systems to be used

CLP – Main processes

- Harmonisation of Classification and Labelling
  - Agreement at EU level on classification
  - List of harmonised C&L (Annex VI, C&L Inventory)
  - Suppliers obliged to classify & label accordingly
- Notification of C&L of substances
- Request for use of an alternative chemical name for a substance in a mixture

Further information

- REACH legislation –link
- CLP—legislation and guidance-- link
- Guidance on Information Requirements and Chemical Safety Assessment
  - Chapter 7.b
    - Appendix 7.8-5 (20 pp)
    - Appended to main guidance on aquatic toxicity testing
    - Evaluation of info
    - Not part of standard requirements => available info
    - No fully validated/approved OECD guidelines

Aim of appendix 7.8-5

- Guidance covers available information beyond the standard information requirements:
  - indicating potential endocrine activity in aquatic organisms (from human health endpoints, molecular structure, or non-standard in vitro assays)
  - providing info on an endocrine mode of action in aquatic organisms
  - providing info on adverse effects on reproduction or development of aquatic organisms

Conclusions

- Registration dossiers under REACH
  - Responsibility for Industry
  - Endocrine disruption
    - Data for Level 1, 4 and 5 of OECD framework partly available
    - ED mechanistic studies beyond standard information requirements
- But:
  - Covered under Authorisation
  - Safety net of Restriction
  - Substance evaluation

Thank you for your attention

These slides represent the opinion of the author and do not necessarily reflect the opinion of the European Chemicals Agency.

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